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SEARCH REQUEST FORM

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Date: 2/20/2000 Requester's Full Name: SABIHA QAZI Examiner #: 74141

Art Unit: 1616 Phone (308) 3910 Serial Number: 09/091,665

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****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Contraceptive process + Kit for female mammals comprising a combination of Gestagen + Estrogen

Inventors (please provide full names): Jan Endrikat et al

Earliest Priority Date: 12/23/95 German 195 49 264.1 12/23/95 PCT/DE96/02486 12/20/96

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known.

For Sequence Searches Only *Please include all pertinent information (parent, grandchild, divisional, or issued patent numbers) along with the appropriate serial number.*

Please Search

Contraceptive

Comprising Combination of

(1) Gestagen (e.g see Cl. 4)

(2) Estrogen

&

Kits

Please See attached Cls.

****

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Date Searcher Picked Up: 2-25-00

Date Completed: 3-7-00

Searcher Prep & Review Time: 40

Online Time: 60

Type of Search

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_____ AA Sequence (#)

_____ Structure (#)

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_____ Litigation

_____ Fulltext

_____ Other

Vendors and Cost

✓ STN _____ Dialog

_____ Questel/Orbit _____ Dr.Link

_____ Lexis/Nexis _____ Westlaw

_____ WWW/Internet

_____ In-house sequence systems (list)

_____ Other (specify)

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=> d his

     (FILE 'HOME' ENTERED AT 07:13:00 ON 02 MAR 2000)

     FILE 'HCAPLUS' ENTERED AT 07:13:03 ON 02 MAR 2000
L1             6 S ENDRIKAT J?/AU
L2             4 S DUSTERBERG B/AU
L3             8 S REILHAC P?/AU
L4             0 S L1 AND L2 AND L3
L5            16 S L1-L4
L6             8 S L5 AND (CONTRACEPT? OR GESTAG? OR ?ESTROGEN?)
                 SELECT RN L6 1-8

     FILE 'REGISTRY' ENTERED AT 07:14:16 ON 02 MAR 2000
L7            24 S E1-24

     FILE 'HCAPLUS' ENTERED AT 07:14:24 ON 02 MAR 2000
L8             6 S L6 AND L7
L9             2 S L6 NOT L8

     FILE 'HCAPLUS, BIOSIS, MEDLINE, EMBASE, SCISEARCH, LIFESCI, WPIDS,
     JICST-EPLUS, BIOBUSINESS, BIOTECHDS' ENTERED AT 07:23:03 ON 02 MAR 2000
L10       327153 S (ESTROGEN OR OESTROGEN)
L11       261150 S GESTAGEN OR GESTODENE OR PROGESTERONE OR LEVONORGESTREL
L12        15592 S CYPROTERONE ACETATE OR CHLORMADINONE ACETATE
L13        10922 S DROSPIRENONE OR DIHYDROSPIRORENONE OR NORETHISTERONE
L14         4156 S NORGESTIMATE OR DESOGESTREL OR 3 KETODESOGESTREL
L15          532 S DIENOGEST
L16        86589 S L10 AND (L11-L15)
L17         7709 S L16 AND CONTRACEPT?
L18         1575 S L17 AND (DAY OR TIME PERIOD OR WEEK)
L19         1193 S L17 AND (METHOD OR PROCESS)
L20          380 S L18 AND L19
L21          445 S L17 AND (10 OR 11 OR 12 OR 13 OR 14 OR 15)(2A)DAY
L22          107 S L17 AND (4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR
12)(2A)DAY
L23          215 S L17 AND (28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR
36)(
L24           35 S L17 AND (40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46)(2A)DAY
L25           91 S L17 AND (4 OR 5 OR 6)(2A)WEEK
L26          327 S L23-L25
L27          113 S L21 AND L26
L28           61 DUP REMOV L27 (52 DUPLICATES REMOVED)
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=> d bib abs

L28 ANSWER 1 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
AN 1998:98327 HCAPLUS
DN 128:158935
TI Progestin/**estrogen** oral **contraceptives**
IN Gast, Michael Jay
PA American Home Products Corporation, USA
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804266	A1	19980205	WO 1997-US12788	19970723
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9739616	A1	19980220	AU 1997-39616	19970723
PRAI	US 1996-688177		19960726		
	WO 1997-US12788		19970723		

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for **28** consecutive **days**, a first phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg **dienogest**, and 250 .mu.g-4 mg **drospirenone**, and an **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 9-**13 days** beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and **estrogen** combination is administered in each of the 9-**13 days**. A second phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg **dienogest**, and 250 .mu.g-4 mg **drospirenone**, and an **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for **11-15 days** beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and **estrogen** combination is administered in each of the **11-15 days**, and an **estrogen** phase **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 3-5 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the **estrogen** is administered in each of the 3-5 days, provided that the daily dosage of second phase progestin is greater than the daily dosage of the first phase progestin and that the daily dosage of the second phase **estrogen**. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, lactose, polacrilin potassium, magnesium

stearate, Opadry pink, polyethylene glycol, and wax.

=> d bib abs 2-61

L28 ANSWER 2 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 3
AN 1998:646576 HCAPLUS
DN 130:20720
TI Effect of two oral **contraceptives** containing ethinyl estradiol and **gestodene** or **norgestimate** on different lipid and lipoprotein parameters
AU Wiegratz, I.; Jung-Hoffmann, C.; Gross, W.; Kuhl, H.
CS Division of Gynecological Endocrinology, Department of Obstetrics and Gynecology, J.W. Goethe-University Frankfurt, Frankfurt, Germany
SO Contraception (1998), 58(2), 83-91
CODEN: CCPTAY; ISSN: 0010-7824
PB Elsevier Science Inc.
DT Journal
LA English
AB The effect of a triphasic oral **contraceptive** contg. ethinyl estradiol and **gestodene** (EE/GSD) on various lipid and lipoprotein parameters was compared with that of a monophasic formulation contg. 35 .mu.g ethinyl estradiol and 250 .mu.g **norgestimate** (EE/NGM). Blood samples were collected from **46** women on **days** 2, **11**, and 21 of the preceding control cycle and of the third, sixth, and twelfth treatment cycles. There was no significant difference between formulations with regard to the influence on any measured parameter. As compared with controls, a significant increase was obsd. in the plasma levels of total triglycerides (24-78%), total phospholipids (7-20%), very low d. lipoprotein (VLDL) triglycerides (61-76%), VLDL-phospholipids (14-60%), low d. lipoprotein (LDL) triglycerides (8-35%), LDL-phospholipids (28-30%), high d. lipoprotein (HDL) cholesterol (8-16%), HDL 3-cholesterol (11-20%), HDL-triglycerides (17-66%), HDL-phospholipids, HDL 3-phospholipids (7-11%), apolipoprotein (apo) A-I (5-20%) and apo A-II (10-40%) during treatment with both formulations. In contrast, the LDL-cholesterol levels were significantly decreased. These changes in lipid metab. appear to reflect a predominance of the effect of the **estrogen** component. The results indicate that both low dose oral **contraceptives** contg. different progestins and different amts. of EE do not exert a deleterious effect on lipoprotein metab., as high HDL-cholesterol and low LDL-cholesterol levels are known as low risk factors of cardiovascular disease. In contrast to endogenous hypertriglyceridemia, an EE-induced rise in triglyceride levels does not appear to increase cardiovascular risk if LDL is not increased.

L28 ANSWER 3 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 4
AN 1998:241132 HCAPLUS
DN 129:36524
TI A regimen of oral **contraceptives** restricted to the periovulatory period may permit folliculogenesis but inhibit ovulation
AU Letterie, Gerard S.
CS Section of Reproductive Endocrinology and Infertility, Department of Obstetrics & Gynecology, Virginia Mason Medical Center, Seattle, WA, USA
SO Contraception (1998), 57(1), 39-44

CODEN: CCPTAY; ISSN: 0010-7824
PB Elsevier Science Inc.
DT Journal
LA English
AB Increased safety of oral **contraceptives** (OC) has resulted from a redn. in the **estrogen** and progestin content per tablet. A redn. in the no. of hormonally active pills and their placement at crit. points within the cycle may provide a novel regimen for further reducing the hormonal content of OC per cycle and their attendant side effects without compromising efficacy. The objective of this study was to det. the effectiveness of two OC regimens that incorporate a delayed start and limited midcycle use of the combination of ethinyl estradiol and norethindrone, and limited use of norethindrone only during the second half of the cycle. Main outcome measures were defined as ovulation, serum concns. of estradiol (E2), LH, FSH, **progesterone** (P), follicular diams., and endometrial thickness. Volunteers were issued blister packs contg. 28 pills and randomized to one of two groups. Group 1 used a combination of 50 .mu.g ethinyl estradiol and 1 mg norethindrone per tablet **day** 6-**10**, and 0.70 mg norethindrone only **day 11**-19. Placebo tablets were used on days 1-5 and **day** 20-**28**. Group 2 used a combination of 50 .mu.g ethinyl estradiol and 1 mg norethindrone per tablet on **day** 8-**12**, and 0.70 mg norethindrone only on **day 13** -21. Placebo tablets were used on day 1-7 and **day** 22-**28** . A total of 20 cycles were studied using 10 volunteers. To assess any possible carryover effect, two successive cycles were studied for each subject. Serum sampling for E2, FSH, LH, and P, and transvaginal ultrasound imaging to assess endometrial thickness and follicle diam. were carried out at 4 day intervals throughout the cycle. One ovulation occurred in 10 cycles in group 1. Five ovulations occurred in 10 cycles in group 2. All ovulations, regardless of group, occurred in the second cycle. Peak E2 concns. were not significantly different between groups (152.04 pg/mL vs. 162.1 pg/mL [mean] for groups 1 and 2, resp.) but occurred earlier in the cycle in group 1. No differences were noted between the groups in serum concns. of FSH or LH for any given cycle day. Max. follicle diams. were not different between groups 1 and 2, regardless of ovulatory status (20.5 Mm2 vs. 20.6 Mm2, resp.). Ultrasound imaging assessment of midcycle follicle growth revealed diams. ranging from 18.5 Mm2 to 34.0 Mm2 with gradual resoln. through the second half of the cycle in anovulatory cycles, and 16.0 Mm2 to 23.5 Mm2 with abrupt disappearance in ovulatory cycles. Endometrial thickness did not exceed 10 mm for any anovulatory cycle regardless of group, but ranged from 6 to 9 and 6 to 11 during the luteal phase of ovulatory cycles of groups 1 and 2, resp. Peak serum P concns. at midluteal phase in ovulatory cycles ranged from 9.2 ng/mL to 18.2 ng/mL. Data from this preliminary study suggest that ovulation may be prevented with a combination of ethinyl estradiol and norethindrone started as late as cycle day 6 and limited to 5 days' duration using norethindrone only for 9 days during the second half of the cycle. Such a restricted regimen may offer both an effective method of **contraception** and a means of further reducing both **estrogen** and progestin content per cycle and the possible short and long term adverse side effects of these hormones.

L28 ANSWER 4 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 5
AN 1997:745952 HCAPLUS
DN 128:26926
TI Oral **contraceptives**
IN Gast, Michael Jay
PA American Home Products Corporation, USA
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9741871	A1	19971113	WO 1997-US7085	19970428
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9729269	A1	19971126	AU 1997-29269	19970428
PRAI	US 1996-647086		19960508		
	WO 1997-US7085		19970428		

AB This invention provides a method of **contraception** which comprises administering to a female of child-bearing age for **28** consecutive **days**, a first phase combination of a progestin at a daily dosage equiv. in progestational activity to 40-125 .mu.g **levonorgestrel** and an **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinylestradiol for 3-8 days beginning on day 1 of the menstrual cycle; a second phase combination of a progestin at a daily dosage equiv. in progestational activity to 40-125 .mu.g **levonorgestrel** and an **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinylestradiol for 4-**15 days**; a third phase combination of a progestin at a daily dosage equiv. in progestational activity to 40-125 .mu.g **levonorgestrel** and an **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinylestradiol for 4-**15 days**; and an **estrogen** phase **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinylestradiol for 3-5 days. The daily dosage of the combination administered in the first phase is not the same as the daily dosage of the combination administered in the second phase and that the daily dosage of the combination administered in the second phase is not the same as the daily dosage of the combination administered in the third phase.

L28 ANSWER 5 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 6
AN 1997:465078 HCAPLUS
DN 127:86120
TI Method and kit for **contraception**
IN Endrikat, Jan; Duesterberg, Bernd; Reilhac, Pia
PA Schering A.-G., Germany
SO Ger. Offen., 7 pp.
CODEN: GWXXBX
DT Patent

LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19549264	A1	19970626	DE 1995-19549264	19951223
	CA 2241192	AA	19970703	CA 1996-2241192	19961220
	WO 9723228	A2	19970703	WO 1996-DE2486	19961220
	WO 9723228	A3	19970828		
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9719219	A1	19970717	AU 1997-19219	19961220
	EP 868188	A2	19981007	EP 1996-946221	19961220
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1205639	A	19990120	CN 1996-199301	19961220
	BR 9612207	A	19990713	BR 1996-12207	19961220
	JP 2000502108	T2	20000222	JP 1997-523223	19961220
	NO 9802902	A	19980622	NO 1998-2902	19980622
PRAI	DE 1995-19549264	19951223			
	WO 1996-DE2486	19961220			

AB A method for **contraception** in female mammals involves administration of an ovulation-inhibiting dose of a **gestagen** daily for .gtoreq.**28 days**, and of a natural **estrogen** for 5-**10 days** at the end of this **28-day** period. This regimen allows regular menstruation-like bleeding combined with reliable control of the ovarian cycle. The **gestagen** may be administered orally and the **estrogen** transdermally, or vice versa. Alternatively, a kit may comprise a 1st phase of 18-23 daily oral doses of **gestagen** and a 2nd phase of 5-10 daily oral doses of a **gestagen-estrogen** combination. For example, **levonorgestrel** was administered for 56 days at 0.1 mg/day; during the last **10 days** of this period, estradiol was addnl. administered at 2.5 mg/day.

L28 ANSWER 6 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 8
AN 1997:390195 HCAPLUS
DN 127:76226
TI Inhibition of ovulation with transdermal estradiol and oral progestogens in perimenopausal women
AU De Leo, Vincenzo; Lanzetta, Danila; Morgante, Giuseppe; De Palma, Patrizia; D'Antona, Donato
CS Dep. Obstetrics & Gynecology, Univ. Siena, Italy
SO Contraception (1997), 55(4), 239-243
CODEN: CCPTAY; ISSN: 0010-7824
PB Elsevier
DT Journal
LA English
AB The effects of 6 mo of combined hormone therapy with transdermal estradiol (0.05 mg/day x 21 days) and different oral progestogens (**10** mg/**day** medroxyprogesterone acetate [MPA] in the last **12**

days, **10** mg/**day** dihydrogesterone in the last **12 days**, and 50 mg/day cyproterone in the first **10 days**), on menopausal symptoms and hypothalamo-pituitary-ovarian function were studied in normal perimenopausal women. The study included 38 perimenopausal women, aged 43-49 yr, with regular cycles of 26-**32 days** in length and menopausal symptoms. Endocrine status was detd. by assay of basal levels of gonadotropins (LH, FSH), E2, and P every week until menstrual bleeding, before and during the first month of therapy. Plasma levels of LH and FSH were suppressed in the first month of therapy while E2 had a mean value of 45.+-.12 pg/mL. Ultrasound examn. and low levels of P indicated a complete block of ovulation and hypothalamo-pituitary-ovarian activity. All women reported the disappearance of vasomotor symptoms and nocturnal sweating. Transdermal estradiol and oral progestogens were well tolerated. This study shows that combined hormone therapy with low doses of transdermal **estrogen** patches and different oral progestogens reduces menopausal symptoms and also safeguards against unwanted pregnancies in the perimenopausal period.

L28 ANSWER 7 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 9
AN 1997:767624 HCAPLUS
DN 128:43960
TI A randomized cross-over study comparing pharmacodynamic and metabolic variables of a new combiphasic and a well-established triphasic oral **contraceptive**
AU Van Den Ende, A.; Geurts, T. B. P.; Kloosterboer, H. J.
CS Laboratory of Special Hematology and Hemostasis, Academic Medical Centre, Amsterdam, Neth.
SO Eur. J. Contracept. Reprod. Health Care (1997), 2(3), 173-180
CODEN: ECRCFK; ISSN: 1362-5187
PB Parthenon Publishing Group Ltd.
DT Journal
LA English
AB In an open-label, randomized, cross-over study in 20 subjects, the short-term effects were investigated of Gracial (DSG/EE 7 .times. 25/**40** .mu.g/**day** + **15** .times. 125/**30** .mu.g/**day**) and Trigynon (LNG/EE 6 .times. 50/**30** .mu.g/**day** + 5 .times. 75/**40** .mu.g/**day** + **10** .times. 125/**30** .mu.g/**day**) on plasma concns. of 17.beta.-estradiol and **progesterone** as well as on carrier proteins (SHBG, CBG, ceruloplasmin), AT-III, carbohydrate metab. (insulin, glucose, glycosylated proteins) and lipid metab. (total cholesterol, triglycerides, phospholipids, HDL-C, LDL-C, HDL2-C, HDL3-C, HDL2-C/HDL3-C ratio, Apo A1, Apo B, Apo A1/Apo B ratio). Both prepns. adequately and similarly inhibited ovulation in all subjects. Serum levels of carrier proteins were significantly higher with DSG/EE than with LNG/EE, whereas no between-group differences were obsd. with respect to fasting glucose and insulin, glycosylated proteins (mainly glycosylated albumin) and AT-III activity. DSG/EE showed significantly higher plasma levels than LNG/EE of **estrogen**-dependent lipid parameters such as triglycerides, HDL-C, HDL2-C, Apo A1, HDL2-C/HDL3-C ratio and Apo A1/Apo B ratio, whereas the levels of LDL-C and Apo B were significantly lower. Both oral **contraceptive** prepns. were equally effective in suppression of follicular development, but combiphasic DSG/EE induced

higher plasma levels of carrier proteins and higher plasma levels of potentially anti-atherogenic lipid parameters than did triphasic LNG/EE.

L28 ANSWER 8 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 10
AN 1997:74241 HCAPLUS
DN 126:113344
TI Effects of daily low dose mifepristone on endometrial maturation and proliferation
AU Cameron, Sharon T.; Critchley, Hilary O.D.; Thong, K.Joo; Buckley, C.Hilary; Williams, Alistair R.; Baird, David T.
CS Department of Obstetrics and Gynaecology, Centre for Reproductive Biology, University of Edinburgh, Edinburgh, EH3 9EW, UK
SO Hum. Reprod. (1996), 11(11), 2518-2526
CODEN: HUREEE; ISSN: 0268-1161
PB Oxford University Press
DT Journal
LA English
AB Following an ovulatory control cycle, six women took 2 mg of mifepristone daily for **30 days**. Endometrial biopsies were collected in the control cycle between 7 and **11 days** after the plasma LH surge and on the corresponding day of the treatment cycle (**days** 19-**28**). In order to investigate the effects of unopposed **estrogen** on the endometrium, persistent proliferative endometrium was obtained from six women with anovulatory infertility due to polycystic ovarian syndrome (PCOS) on a similar cycle day (days 21-23) following a progestogen-induced withdrawal bleed. Endometrium was evaluated for histol. and immunolocalization of **estrogen** receptors (ER), **progesterone** receptors (PR) and the cell proliferation markers [proliferating cell nuclear antigen (PCNA) and Ki67]. Treatment with mifepristone inhibited ovulation in four of the six subjects. In the two subjects in whom ovulation did occur, secretory transformation was delayed, suggesting that successful implantation of a blastocyst would be unlikely. In subjects who remained anovulatory during treatment, the histol. and pattern of steroid receptor expression was similar to proliferative phase endometrium. In women with PCOS, mitoses and intense immunostaining for ER, PR and cell proliferation markers were obsd. in both glands and stroma. Although PCNA and Ki67 immunostaining were also present in mifepristone-treated endometrium from subjects who did not ovulate, there were no mitoses and significantly less ER immunostaining in spite of exposure to unopposed **estrogen** for a similar duration. Since PCNA and Ki67 detect cells throughout all stages of the cell cycle this would suggest that mifepristone might affect the entry of cells into the mitotic phase of the cell cycle and, therefore, might prevent endometrial hyperplasia. These findings add further evidence to support the **contraceptive** potential and antiproliferative activity of daily low dose mifepristone.

L28 ANSWER 9 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 12
AN 1996:2828 HCAPLUS
DN 124:45923
TI Failure of **estrogen** induced luteinizing hormone surge in women treated with mifepristone (RU 486) every **day** for **30 days**
AU Baird, David T.; Thong, K. J.; Hall, C.; Cameron, S. T.

CS Centre Reproductive Biology, University Edinburgh, Edinburgh, EH3 9EW, UK
SO Hum. Reprod. (1995), 10(9), 2270-6
CODEN: HUREEE; ISSN: 0268-1161
DT Journal
LA English
AB It has been demonstrated previously that administration of the antiprogestin mifepristone (RU 486; 1-5 mg daily) inhibits or delays both the pre-ovulatory LH surge and ovulation. To investigate this mechanism, dynamic tests of pituitary ovarian function were performed in six healthy women before and during the administration of mifepristone (2 mg daily for **30 days**). On day 9 of the control and treatment cycles, samples of blood were collected every 15 min over 12 h for measurement of LH concn. After 10 h, the responsiveness of the pituitary was tested by the i.v. injection of 10 .mu.g of gonadotropin-releasing hormone (GnRH). On **day 10** of the control and treatment cycles, two patches releasing 200 .mu.g/day of estradiol were applied to skin on the abdomen for 3 days. Blood was collected at 24, 48, 59, 72, 81 and 96 h after application of the **estrogen** patches for the measurement of gonadotropin and ovarian hormone concns. Follicular development continued in all women during their treatment with mifepristone, and ovulation was suppressed (four women) or delayed (two women). There was no significant difference in the basal concn. of LH between the control and treatment cycles (5.5 vs. 7.7 IU/l resp.), or in the frequency (interpulse interval, 101 vs. 105 min resp.) and the amplitude (2.1 vs. 2.6 IU/l resp.) of LH pulses. The response to GnRH was similar. On **day 10**, the basal concns. of LH, FSH, prolactin, estradiol and **progesterone** and the diam. of the dominant follicle (15.7 vs. 13.3 mm) were similar during control and treatment cycles. In control cycles, there were significant increases in the concns. of LH and FSH within 72 h of application of the **estrogen** patches. During treatment cycles, concns. of FSH and LH remained low, and were significantly lower than the values obsd. during control cycles. The authors conclude that the antiprogestin mifepristone disrupts ovulation by inhibiting the pos. feedback effect of **estrogens** and, hence, prevents or delays the generation of a pre-ovulatory LH surge.

L28 ANSWER 10 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 14
AN 1994:401236 HCAPLUS
DN 121:1236
TI Pharmacological properties of the modified **estrogen** 9.alpha.,11.beta.-dioxyestrone 3-acetate-11-nitrate
AU Ivanenko, T. I.; Pokrovskaya, Ye. V.; Rzheznikov, V. M.; Fedotov, V. P.
CS Inst. Exp. Endocrinol., Moscow, 117036, USSR
SO Eksp. Klin. Farmakol. (1994), 57(2), 36-9
CODEN: EKFAE9; ISSN: 0869-2092
DT Journal
LA Russian
AB The expts. on 715 adult non-inbred female rats and 11 Wistar male rats have established that the **estrogen** 9.alpha.,11.beta.-dioxyestrone 3-acetate-11-nitrate (NDE-As) has an oral **contraceptive** activity which is equal to ethynylestradiol (EE). A combined **14-day** administration of NDE-As with various **gestagens** produces a higher **contraceptive** effect that does EE used in combination with the same **gestagens**. A

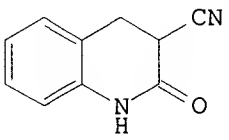
30-day use of NDE-As combined with acetomepregenol (AMP) results in a more significant and prolonged secretion of LH than does the EE-AMP combination. Unlike ethynylestradiol, NDE-As has no hypertriglyceridemic effect when given in oral doses of 0.25 and 1.25 mg/kg body wt.

L28 ANSWER 11 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 15
AN 1992:228421 HCAPLUS
DN 116:228421
TI **Contraceptives** containing **desogestrel** or **levonorgestrel** have different effects on serum lipoproteins and post-heparin plasma lipase activities
AU Kauppinen-Makelin, Ritva; Kuusi, Timo; Ylikorkala, Olavi; Tikkanen, Matti J.
CS 3rd Dep. Med., Univ. Helsinki, Helsinki, Finland
SO Clin. Endocrinol. (Oxford) (1992), 36(2), 203-9
CODEN: CLECAP; ISSN: 0300-0664
DT Journal
LA English
AB The effects of mono and polyphasic oral **contraceptives** contg. **desogestrel** or **levonorgestrel** on serum lipoproteins, sex hormone binding globulin and post-heparin plasma lipase activities were investigated. Healthy women took either **desogestrel** or **levonorgestrel** during the first menstrual cycle on **days 15-28**. They then received monophasic ethinylestradiol plus either **desogestrel** or **levonorgestrel** for three cycles. After this, the women took sequential pills contg. ethinylestradioll plus either **desogestrel** or **levonorgestrel** for the three following cycles. **Desogestrel** (150 .mu.g/day) did not change serum total triglyceride concn., whereas **levonorgestrel** (150 .mu.g/day) decreased it. Except for monophasic ethinylestradiol plus **levonorgestrel**, the **estrogen**-contg. combinations increased serum triglyceride level. Low d. lipoprotein (LDL) cholesterol remained stable with all treatments, but the cholesterol/triglyceride ratio of LDL decreased during all combinations with ethinylestradiol. **Levonorgestrel** reduced total high d. lipoprotein (HDL) cholesterol and both progestins reduced HDL2 cholesterol concn. Addn. of ethinylestradiol reversed this change in the **desogestrel** but not in the **levonorgestrel** group. The polyphasic ethinylestradiol plus **levonorgestrel** combination did not change total HDL cholesterol. Hepatic lipase was activated with either progestin when administered alone but its activity was suppressed below the baseline level when ethinylestradiol was added. Conversely, both progestins suppressed sex hormone binding globulin levels, but addn. of ethinylestradiol caused marked increases above baseline. These increases were greater in women taking **desogestrel** than in those taking **levonorgestrel**. No treatment affected lipoprotein lipase activity. Thus, monophasic or polyphasic combinations of ethinylestradiol and **desogestrel** do not have deleterious effects on serum lipoproteins. If **levonorgestrel** is used as the progestin component, polyphasic ethinylestradiol plus **levonorgestrel** appears more favorable than monophasic ethinylestradiol plus **levonorgestrel**.

L28 ANSWER 12 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 17

AN 1988:739 HCAPLUS
DN 108:739
TI Use of tamoxifen, an antiestrogen, in establishing a need for **estrogen** in early pregnancy in the bonnet monkey (Macaca radiata)
AU Ravindranath, N.; Moudgal, N. R.
CS Cent. Adv. Res. Reprod. Biol., Indian Inst. Sci., Bangalore, 560 012, India
SO J. Reprod. Fertil. (1987), 81(2), 327-36
CODEN: JRPFA4; ISSN: 0022-4251
DT Journal
LA English
AB Administration of tamoxifen orally (3 mg/kg/day) during the postovulatory period on days 16-20 or **days** 18-**30** of female bonnet monkeys mated on **days** 9-**14** of the cycle resulted in inhibition of establishment of pregnancy in 90-100% of monkeys tested. The establishment of pregnancy in control female monkeys after exposure to the male during 1 ovulatory cycle was 66%. The effect of tamoxifen was not due to interference with luteal function because there was no redn. in serum **progesterone** concns. after drug treatment. Exogenously administered **progesterone** could not reverse the inhibitory effect of tamoxifen on establishment of pregnancy. The effect of tamoxifen was dose dependent. Tamoxifen could be developed as an effective postovulatory **contraceptive** for regulation of female fertility.

L28 ANSWER 13 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 18
AN 1988:32121 HCAPLUS
DN 108:32121
TI **Contraceptive** and hormonal properties of a new 1,4-dihydro-2-oxoquinoline derivative (compound 84-182) in rodents and rhesus monkeys
AU Singh, M. M.; Mehrotra, P. K.; Agnihotri, A.; Srivastava, Ranjan P.; Seth, M.; Bhaduri, A. P.; Kamboj, V. P.
CS Div. Endocrinol., Cent. Drug Res. Inst., Lucknow, 226001, India
SO Contraception (1987), 36(2), 239-51
CODEN: CCPTAY; ISSN: 0010-7824
DT Journal
LA English
GI

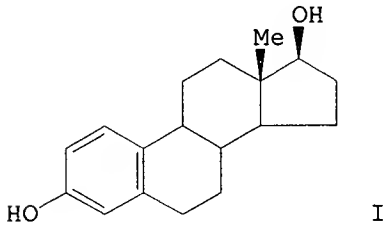


I

AB Compd. 84-182 (I) prevented pregnancy when administered s.c. at a 10-mg/kg dose on days 3-8 post coitum in hamsters and on **days** 6-**10** post coitum in guinea pigs. At lower doses, although in hamsters there was a marked redn. in implantation no., the majority of

implantations in guinea pigs showed signs of resorption. I was ineffective when administered at a 10-mg/kg dose on days 1-3 or 6-7 post coitum in hamsters and on days 1-5 or 4-8 post coitum in rats. In rhesus monkeys, treatment with the compd. at 5- and 10-mg/kg doses on days 16-21 of the menstrual cycle induced frank vaginal bleeding between days 21 and 24. Treatment on **days** 21-**30** or after confirmation of pregnancy on **days 32-36** was ineffective. In conventional bioassays, I was devoid of any estrogenic, antiestrogenic, progestational, antiprogestational, androgenic, or antiandrogenic properties at the **contraceptive** dose. In a competitive protein binding assay, I showed a relative binding affinity (RBA) of <0.1% and 0.28% of **progesterone**, resp., for rabbit and hamster uterine cytosol **progesterone** receptors. Its RBA for rat uterine cytosol **estrogen** receptors was <0.1% of 17.beta.-estradiol.

L28 ANSWER 14 OF 61 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 20
AN 1983:416668 HCAPLUS
DN 99:16668
TI Evaluation of a rapid method for determination of total urinary **estrogens** in morning samples from normally menstruating women
AU Fleetwood, Louise; Zheng, Shu Rong; Eneroth, P.; Landgren, B. M.
CS Dep. Obstet. Gynecol., Karolinska Hosp., Stockholm, S-104 01, Swed.
SO Contraception (1983), 27(4), 329-38
CODEN: CCPTAY; ISSN: 0010-7824
DT Journal
LA English
GI



I

AB Total urinary **estrogens** (TUE) in morning urine samples delivered during 7 days around midcycle from 14 normally menstruating women were analyzed by RIA, and the results were compared with those obtained by RIA of serum 17.beta.-estradiol (I) [50-28-2] and LH [9002-67-9]. The Spinnbarkeit of the cervical mucus was also detd. daily and ovulation was confirmed by RIA of serum **progesterone** [57-83-0]. Significant correlations between day of peak levels of serum I and the day with the highest TUE value were obtained. Peak values for Spinnbarkeit, I, TUE, and LH were on the av. obtained on cycle **day 13**.1 (**10**-17), 13.3 (10-16), 13.9 (11-18), and 14.1 (11-17), resp., and the mean cycle length was 27.9 (24-**32**) **days**. The difference in mean peak day for I and TUE, I and Spinnbarkeit, and I and LH was significant in each comparison. Assays of TUE in morning samples as compared to anal. of TUE in 24-h urine portions were compared during 48 h in 10 women. The day with the highest TUE excretion was the same in 7 women irresp. of the type of urinary sample analyzed. Anal. of urinary

creatinine did not improve the TUE results. Levels of TUE in normally cycling females, in women taking **contraceptive** steroids, in menopausal women, and in normal men agreed with those previously reported.
The TUE detn. by RIA may be helpful as a rapid method for everyday clin. use.

L28 ANSWER 15 OF 61 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:219991 HCAPLUS
DN 130:242332
TI Oral **contraceptive** preparation having a first phase comprising progestin/**estrogen** and a second phase comprising progestin
IN Gast, Michael Jay
PA American Home Products Corporation, USA
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9913882	A1	19990325	WO 1998-US18850	19980909
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9892286	A1	19990405	AU 1998-92286	19980909

PRAI US 1997-928530 19970912
WO 1998-US18850 19980909
AB A method of **contraception** comprises administering to a female of child-bearing age for **28 days** per menstrual cycle a combination of a progestin at a daily dosage equiv. to 30-150 .mu.g **levonorgestrel** and an **estrogen** at a daily dosage equiv. to 10-20 .mu.g ethynylestradiol for 23-25 days beginning on day 1 of the menstrual cycle, followed by administering a progestin at a daily dosage equiv. to 10-100 .mu.g **levonorgestrel** for 3-5 days. This regimen provides effective **contraception**, good cycle control, and minimal side effects while greatly reducing the total **contraceptive** steroid administered per **28-day** cycle. A suitable regimen comprised administration of **levonorgestrel** 75 and ethynylestradiol **15** .mu.g/**day** for the first 24 cycle days, followed by **levonorgestrel** 37.5 .mu.g/day for the last 4 days.

L28 ANSWER 16 OF 61 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:282399 HCAPLUS
DN 128:326539
TI Triphasic combination of progestin/**estrogen** female oral **contraceptives**
IN Gast, Michael J.
PA American Home Products Corp., USA
SO U.S., 8 pp.
CODEN: USXXAM

DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5747480	A	19980505	US 1997-839286	19970417

AB This invention provides a method of **contraception** which comprises administering to a female of child bearing age for **28** consecutive **days**, a first phase combination of a progestin at a daily dosage equiv. in progestational activity to 40-125 .mu.g **levonorgestrel** and an **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinylestradiol for 3-8 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and **estrogen** combination is administered in each of the 3-8 days, a second phase combination of a progestin at a daily dosage equiv. in progestational activity to 40-125 .mu.g **levonorgestrel** and an **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinylestradiol, for 4-**15 days** beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and **estrogen** combination is administered in each of the 4-**15 days**. A third phase combination of a progestin at a daily dosage equiv. in progestational activity to 40-125 .mu.g **levonorgestrel** and an **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinylestradiol, for 4-**15 days** beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the progestin and **estrogen** combination is administered in each of the 4-**15 days**, and an **estrogen** phase **estrogen** at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinylestradiol, for 3-5 days beginning on the day immediately following the last day of administration of the third phase combination, wherein the same dosage of the **estrogen** is administered in each of the 3-5 days, provided that the daily dosage of the combination administered in the first phase is not the same as the daily dosage of the combination administered in the second phase and that the daily dosage of the combination administered in the second phase is not the same as the daily dosage of the combination administered in the third phase. This invention also provides a **contraceptive** kit adapted for daily oral administration for the total no. of 28 combination dosage units.

L28 ANSWER 17 OF 61 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:240103 HCAPLUS
DN 122:17220
TI Multiphase hormonal system for **contraception**
IN Moore, Claudia; Oettel, Michael
PA Jenapharm GmbH, Germany
SO Ger. Offen., 10 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4313926	A1	19941103	DE 1993-4313926	19930428

AB The title system comprises combinations of **estrogens** and a **gestagen** to be administered during the 1st 3 phases of the ovarian cycle and an **estrogen** prepn. to be applied in the 4th phase. Thus, film tablets were provided for administration on the following days of the ovarian cycle contg., in addn. to std. excipients, the following active agents (in mg): days 1-7, ethynylestradiol (I) 0.050, **levonorgestrel** (II) 0.010, estradiol valerate (III) 1.000; **days** 8-**14**, I 0.075, II 0.050, III 1.000; **days** **15**-21, I 0.005, II 0.075, III 1.000; **days** 22-**28** , III 1.000.

L28 ANSWER 18 OF 61 HCAPLUS COPYRIGHT 2000 ACS
AN 1989:527206 HCAPLUS
DN 111:127206
TI **Contraceptive** potential of RU 486 by ovulation inhibition: I. Pituitary versus ovarian action with blockade of **estrogen** -induced endometrial proliferation
AU Van Uem, Jan F. H. M.; Hsiu, Jeng G.; Chillik, Claudio F.; Danforth, Douglas R.; Ulmann, Andre; Baulieu, Etienne E.; Hodgen, Gary D.
CS Erlangen, 8520, Fed. Rep. Ger.
SO Contraception (1989), 40(2), 171-84
CODEN: CCPTAY; ISSN: 0010-7824
DT Journal
LA English
AB In previous studies, RU 486 administration arrested spontaneous folliculogenesis. To investigate the central vs. peripheral effects on RU 486 on the ovarian/menstrual cycle, including endometrial proliferation, RU 486 was administered daily (**10** mg/kg/**day**, i.m.) from menstrual cycle day 3 or 7 to day 25 in normal adult cynomolgus monkeys (Macaca fascicularis) receiving human menopausal gonadotropin (hMG) treatment (37.5 IU/day) from days 3-8. RU 486 administration with hMG/human chorionic gonadotropin (hCG) therapy did not inhibit ovarian response, as evidenced by steroidogenesis and ovulation. Nine of 23 oocytes retrieved by lavage or follicular aspiration at laparotomy after ovulation induction were morphol. classified as mature preovulatory status. Whereas an endometrial biopsy performed on cycle day 25 in control monkeys revealed an in phase mature secretory endometrium, histol. sections from RU 486 plus hMG/hCG-treated females uniformly demonstrated atrophic to weakly proliferative endometrium on cycle day 25, despite serum estradiol levels >300 pg/mL. Three months after the initial 25-day study, endometrial biopsies revealed persistent atrophic endometrium, even though repeated ovulation induction with hMG/hCG therapy elevated serum **estrogen** concns. The findings prevailed whether RU 486 treatment began on cycle day 3 or 7. The intermenstrual interval was significantly lengthened by RU 486 treatments (**28**.5 **days**, control vs. 131.3 days, RU 486). In summary, RU 486 consistently blocked ovulation unless hCG was provided and elicited a persistent retardation of early proliferative endometrium when administered daily beginning in early or mid-follicular phase. The normal mitogenic effects of elevated ovarian **estrogen** secretion on endometrial tissue were quelled, uniformly resulting in amenorrhea. The long-lasting action of RU 486, causing

ovulation inhibition and atrophic endometrium, may be due to the depot effect of i.m. injection. In addn., RU 486 did not prevent ovarian steroidogenesis, ovulation, or oocyte maturation when an ovulation induction regimen of hMG/hCG was given. Apparently, RU 486 prevented ovulation by diminishing pituitary gonadotropin secretion, rather than by direct effects on ovarian folliculogenesis, and induced amenorrhea by inhibiting **estrogen**-induced endometrial proliferation.

L28 ANSWER 19 OF 61 HCAPLUS COPYRIGHT 2000 ACS
AN 1988:543029 HCAPLUS
DN 109:143029
TI Thyroid hormone profile in normally menstruating women
AU Alakananda, Kumari; Gogoi, P.; Gogoi, M. P.
CS India
SO J. Obstet. Gynaecol. India (1988), 38(3), 327-30
CODEN: JOBYA4; ISSN: 0022-3190
DT Journal
LA English
AB Thyroid hormones in the blood serum of women showed cyclical variations during the ovarian cycle, being higher in the luteal phase (**15-30 days**) than in the follicular phase (1-**14 days**). Both T4 and T3 were maximal around the time of ovulation. Thyroid hormone levels in women on oral **contraceptives** were higher than those in nonpregnant women not taking **contraceptives**, irresp. of the menstrual phase. The cyclical variations of thyroid hormones during the ovarian cycle were related to the effects of **estrogen** and **progesterone**, with the max. level of thyroid hormones coinciding with the pre-ovulatory peak of **estrogen** and the high levels in the luteal phase corresponding to the mid-luteal rise in **progesterone**.

L28 ANSWER 20 OF 61 HCAPLUS COPYRIGHT 2000 ACS
AN 1984:417583 HCAPLUS
DN 101:17583
TI Endometrial changes after long-term use of continuous **estrogen** and cyclic progestogen
AU Fink, B. J.
CS Dep. Gynaecol. Obstetr., Frederiksborg Cty. Hosp., Hilleroed, DK 3400, Den.
SO Maturitas (1984), 5(4), 277-80
CODEN: MATUDK; ISSN: 0378-5122
DT Journal
LA English
AB Eight women with primary failure of ovarian function and 12 women undergoing the climacteric were treated sequentially with estradiol-estriol and **norethisterone** acetate (Trisequens [66100-41-2]). After a mean treatment period of 5 yr (range 3-8 yr), endometrial biopsies were taken on **day 11** or **12** at the end of an **estrogen**-only phase. All biopsies showed the presence of a proliferative endometrium without any signs of hyperplasia or carcinoma in situ. Although cyclic **estrogen** therapy can cause hyperplasia, a small dose of a progestogen (**norethisterone** acetate) for **10 days** in a **28-day** cycle can prevent hyperplasia of the endometrium during long-term treatment.

L28 ANSWER 21 OF 61 HCAPLUS COPYRIGHT 2000 ACS

AN 1984:544361 HCAPLUS
DN 101:144361
TI The efficacy of triphasic oral **contraceptives** and effects on the pituitary-ovarian axis in younger women compared with other types of oral **contraceptives**
AU De Cecco, Luigi; Capitanio, Gianluigi; Venturini, Pierluigi; Tuo, Federico; Marzetti, Luigi; Gherardi, Silvio
CS Inst. Obstet. Gynecol., Univ. Genoa, Genoa, Italy
SO New Consid. Oral Contracept., Proc. Int. Symp. (1982), Meeting Date 1981, 191-208. Editor(s): Brosens, Ivo. Publisher: Biomed. Inf. Corp. Publ., New York, N. Y.
CODEN: 52IWAF
DT Conference
LA English
AB Trinordiol [39366-37-5] is a triphasic oral **contraceptive** formulation of **levonorgestrel** and ethinylestradiol in which the **levonorgestrel** doses increase from 50 .mu.g/day for the 1st 6 days of the ovarian cycle to 75 .mu.g/day for the next 5 days, and then to 125 .mu.g for the remaining **10 days** and ethinylestradiol doses are **30** .mu.g/**day** for the 1st 6 **days**, **40** .mu.g/**day** for the next 5 **days**, and **30** .mu.g/**day** for the remaining **10 days**. The efficacy of Trinordiol and its effects on the pituitary-ovarian axis were compared with those of the progestogen-only minipill quingestanol acetate [3000-39-3] (300 .mu.g) and with another ethinylestradiol-**levonorgestrel** mixt. (50 .mu.g and 0.5 mg) in adolescent girls. No pregnancies occurred, and the side effects encountered with Trinordial were comparable or fewer than with the other agents. The blood LH [9002-67-9], FSH [9002-68-0], estradiol [50-28-2] and **progesterone** [57-83-0] levels were lowered in response to both the triphasic and the combination **contraceptives**; however, the degree of lowering was less in the group treated with the triphasic **contraceptive**. The FSH and LH secretion response to LH-RH [9034-40-6] (100 .mu.g) was the same in progestogen-only group and in controls, was decreased in the triphasic **contraceptive**-treated group, and was abolished in the group treated with the ethinylestradiol-**levonorgestrel contraceptive**. In response to an addnl. 500 .mu.g LH-RH (i.v.), the gonadotropin response was still inhibited in the group treated with ethinylestradiol-**levonorgestrel contraceptive**, but was reestablished in the triphasic **contraceptive**-treated group. After the cessation of **contraceptive** treatment, the LH secretion response to LH-RH in the triphasic group was similar to untreated controls, whereas the response was low in the group treated with ethinylestradiol-**levonorgestrel contraceptive** up to **14 days** and comparable to the triphasic **contraceptive**-treated group by **15**-21 **days**. The advantages of the low-**estrogen** triphasic **contraceptive** in adolescent girls owere discussed.

L28 ANSWER 22 OF 61 HCAPLUS COPYRIGHT 2000 ACS
AN 1984:563869 HCAPLUS
DN 101:163869
TI Implications and assessment of metabolic effects of oral **contraceptives**
AU Briggs, Michael H.
CS Dep. Hum. Biol., Deakin Univ., Victoria, Australia

SO New Consid. Oral Contracept., Proc. Int. Symp. (1982), Meeting Date 1981, 131-51. Editor(s): Brosens, Ivo. Publisher: Biomed. Inf. Corp. Publ., New York, N. Y.
CODEN: 52IWAF
DT Conference
LA English
AB Formulations contg. **levonorgestrel** and ethinylestradiol [39366-37-5] at resp. levels of 250 and 50; 150 and 30; 50 and 50 (for **10 days**) and 125 and 50 (for **11 days**); and 50 and **30** (for 6 **days**), 75 and **40** (for 5 **days**), and 125 .mu.g and 30 .mu.g (for **10 days**) were tested for their long-term metabolic effects in women, and in addn., the changes in biochem. parameters were detd. when women were switched from one of the formulations to a product contg. **desogestrel** (150 .mu.g) plus ethinylestradiol (30 .mu.g) [71138-35-7]. High-dose oral **contraceptives** combining **levonorgestrel** and ethinylestradiol led to changes in the plasma renin [9015-94-5], renin substrate [11002-13-4], antithrombin [9000-94-6] III, plasminogen [9001-91-6], factor X [9001-29-0], factor VIII [9001-27-8], factor VII [9001-25-6], fibrinogen, HDL-cholesterol, cholesterol [57-88-5], triglycerides, and insulin [9004-10-8], and in the glucose [50-99-7] tolerance test. The changes appeared by the end of the 1st treatment cycle, and the magnitude of the changes was dependent on the formulation and also on the duration of treatment. Thus, max. metabolic impact resulted from use of high doses of both **estrogen** and progestogen and min. changes were seen with low doses and with the formulation contg. 250 .mu.g levonorestrel plus 50 .mu.g ethynlestradiol. Changing women to the prepn. contg. **desogestrel** had no significant effect for the 1st 2 cycles on plasma sex hormone-binding globulin, testosterone [58-22-0], 5.alpha.-dihydrotestosterone [521-18-6], or on HDL-cholesterol.

L28 ANSWER 23 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
AN 1999:292760 BIOSIS
DN PREV199900292760
TI Time of implantation of the conceptus and loss of pregnancy.
AU Wilcox, Allen J. (1); Baird, Donna Day; Weinberg, Clarice R.
CS (1) Epidemiology Branch, MD A3-05, NIEHS, Research Triangle Park, NC, 27709 USA
SO New England Journal of Medicine, (June 10, 1999) Vol. 340, No. 23, pp. 1796-1799.
ISSN: 0028-4793.
DT Article
LA English
SL English
AB Background Implantation of the conceptus is a key step in pregnancy, but little is known about the time of implantation or the relation between the time of implantation and the outcome of pregnancy. Methods We collected daily urine samples for up to six months from 221 women attempting to conceive after ceasing to use **contraception**. Ovulation was identified on the basis of the ratio of urinary **estrogen** metabolites to **progesterone** metabolites, which changes rapidly with luteinization of the ovarian follicle. The time of implantation was

defined by the appearance of chorionic gonadotropin in maternal urine. Results There were 199 conceptions, for 95 percent of which (189) we had sufficient data for analysis. Of these 189 pregnancies, 141 (75 percent) lasted at least six weeks past the last menstrual period, and the remaining 48 pregnancies (25 percent) ended in early loss. Among the pregnancies that lasted **6 weeks** or more, the first appearance of chorionic gonadotropin occurred 6 to **12 days** after ovulation; 118 women (84 percent) had implantation on day 8, 9, or 10. The risk of early pregnancy loss increased with later implantation (P<0.001). Among the 102 conceptuses that implanted by the ninth **day, 13** percent ended in early loss. This proportion rose to 26 percent with implantation on **day 10**, to 52 percent on **day 11**, and to 82 percent after **day 11**. Conclusions In most successful human pregnancies, the conceptus implants 8 to **10 days** after ovulation. The risk of early pregnancy loss increases with later implantation.

L28 ANSWER 24 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 7
AN 1997:394470 BIOSIS
DN PREV199799693673
TI Impact of menstrual phase on false-negative mammograms in the Canadian National Breast Screening Study.
AU Baines, Cornelia J. (1); Vidmar, Marjan; McKeown-Eyssen, Gail; Tibshirani, Robert
CS (1) Dep. Public Health Sci., Univ. Toronto, 12 Queen's Park Crescent W., 3rd Flr., Toronto, ON M5S 1A8 Canada
SO Cancer, (1997) Vol. 80, No. 4, pp. 720-724.
ISSN: 0008-543X.
DT Article
LA English
AB BACKGROUND: The efficacy of breast carcinoma screening should be enhanced if false-negative mammography were reduced. Prospectively collected data from the Canadian National Breast Screening Study were used to examine whether menstrual cycle phase was associated with false-negative outcomes for mammographic screening. METHODS: Of 8887 women ages 40-44 years at the onset of screening, randomized to receive annual mammography and clinical breast examination, reporting menstruation no more than **28 days** prior to their screening examination, and with a valid radiologic report, 1898 had never used oral **contraceptives** or replacement **estrogen** with or without **progesterone**. The remainder were past (6573) and current (416) **estrogen** users. Similar selection criteria were applied at subsequent screens. The distribution of false-negative and false-positive mammography in relation to true-negative and true-positive mammography was examined with respect to the follicular (**Days** 1 to **14**) and luteal (**Days 15-28**) menstrual phases. RESULTS: Comparing luteal with follicular mammograms in 6989 patients who ever used **estrogen**, the unadjusted odds ratio (2-sided P-values) for false-negatives versus true-negatives was 2.16 (0.05) and the adjusted odds ratio was 1.47 (0.05). In 1898 never-users, parallel odds ratios for luteal false-negatives were 0.55 (1.0) and 0.74 (1.0), respectively. CONCLUSIONS: These results suggest that menstruating women who have used hormones may have an increased risk of false-negative results for

screening mammograms performed in the luteal phase of the menstrual cycle.
An increased risk of false-negative mammography might adversely affect screening efficacy. The impact of menstrual phase on mammographic interpretation, especially for women who ever used hormones, requires further investigation.

L28 ANSWER 25 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 11
AN 1996:195443 BIOSIS
DN PREV199698751572
TI The effect of **oestrogen** dose and progestogen type on haemostatic changes in women taking low dose oral **contraceptives**.
AU Norris, L. A. (1); Bonnar, J.
CS (1) Dep. Obstet. Gynaecol., Trinity Centre Health Sci., St. James's Hosp.,
Dublin 8 Ireland
SO British Journal of Obstetrics and Gynaecology, (1996) Vol. 103, No. 3, pp.
261-267.
ISSN: 0306-5456.
DT Article
LA English
AB Objective: To determine the effect of **oestrogen** dose and progestogen type on the coagulation and fibrinolytic systems of a group of
normal healthy women taking three different oral **contraceptive** combinations. Design: Plasma levels of factor VII, X, antithrombin III, protein C, fibrinogen, tissue plasminogen activator activity, plasminogen activator inhibitor I antigen and fibrin (D-dimer) degradation products were measured at pretreatment, **6**, 14, 22 **weeks** of treatment and at **6 weeks** post-treatment in a group of 67 women taking either 30 mu-g ethinyloestradiol/150 mu-g **desogestrel** (n = 21), 20 mu-g ethinyloestradiol/150 mu-g **desogestrel** (n = 24), 30 mu-g ethinyloestradiol/75 mu-g **gestodene** (n = 22). Participants: Sixty-seven healthy normal women, 18 to 34 years, smoking fewer than **15** cigarettes per **day**. The subjects were within 10% of their normal body weight and had no history of thromboembolic disease. Setting: Coombe Women's Hospital
and St James's Hospital, Dublin, Ireland. Results: Factor VII and X levels
were significantly raised on treatment with both the 30 mu-g ethinyloestradiol/**desogestrel** and **gestodene** combinations. Higher levels of factor VII activity were observed in the 30
mu-g ethinyloestradiol/**desogestrel** combination compared with the **gestodene** combination. Factor VII and X were not significantly affected by the 20 mu-g ethinyloestradiol combination. Increased plasminogen, fibrinogen and D-dimer levels and decreased plasminogen activator inhibitor I antigen levels were observed during the treatment phases in all three groups. Antithrombin III and protein C activity did not change during treatment with any of the oral **contraceptives** studied. Conclusions: Low dose oral **contraceptives** cause an activation of the coagulation system which is balanced by an activation of
the fibrinolytic system. Reducing the dose of ethinyloestradiol from 30 mu-g to 20 mu-g reduces the effect on factor VII and X. This effect can be

modified by the progestogen. The lesser effect of the 20 mu-g combination may make this a safer option for some women than pills containing a higher dose of **oestrogen**.

L28 ANSWER 26 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 13
AN 1994:231289 BIOSIS
DN PREV199497244289
TI Pharmacodynamic effects of once-a-month combined injectable **contraceptives**.
AU Sang, Guo-Wei
CS Family Planning Res. Inst. Zhejiang, Zhejiang Acad. Med. Sci., Hangzhou 310013 China
SO Contraception, (1994) Vol. 49, No. 4, pp. 361-385.
ISSN: 0010-7824.
DT Article
LA English
AB The pharmacology and clinical assessment of existing first generation once-a-month combined injectable **contraceptives**, mainly Deladroxate and Chinese Injectable No. 1, are reviewed. Although these two types of monthly injectables have been used in some million women in China and Latin America, Deladroxate needs in-depth re-evaluation of its long-term toxicity and possible accumulation. For Injectable No. 1, its disadvantage of being administered on an erratic schedule will cause significant confusion in family planning practice. When used in a strict once-a-month schedule, it is not sufficiently effective for **contraception**. In order to attain predictable menstrual cycle control as well as high efficacy with a **30-day** injection schedule, two improved once-a-month injectable formulations, Cyclofem and Mesigyna, were developed. Pharmacokinetic/pharmacodynamic study on estrogenic components suggested that estradiol valerate and cypionate were suitable **estrogen** esters to give elevated plasma **estrogen** levels for 7 to **11 days**. After a single injection of Cyclofem and Mesigyna, both formulations showed equal **contraceptive** effect with inhibition of follicle maturation for some **30 days** and ovulation, corpus luteum formation for some 60 days. Multicentre studies in the optimization of dosages of progestogens and **estrogens** in once-a-month injectables confirmed that the full doses of Cyclofem (DMPA 25 mg/estradiol cypionate 5 mg) and Mesigyna (NET-EN 50 mg/estradiol valerate 5 mg) are suitable for large scale clinical trials. Pharmacodynamics and progestogen/**estrogen** ratio study indicated the importance of not only the absolute amounts of the progestogen and **estrogen** but also of their ratio. Reduction of **estrogen** dose resulted in break-through ovulation with both Cyclofem and Mesigyna. Also, it is important to note that the second part of the injection cycle is dominated by the progestogen component of both monthly formulations. A longitudinal study indicated that there is no accumulation of **norethisterone** after 12 months of treatment with NET-EN 50 mg and estradiol valerate 5 mg.

L28 ANSWER 27 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 16
AN 1989:9310 BIOSIS
DN BA87:9310
TI THE EFFECT OF RU-486 ADMINISTERED DURING THE PROLIFERATIVE AND SECRETORY PHASE OF THE CYCLE ON THE BLEEDING PATTERN HORMONAL PARAMETERS AND THE

ENDOMETRIUM.
AU SWAHN M L; JOHANNISSON E; DANIORE V; DE LA TORRE B; BYGDEMAN M
CS DEP. OBSTET. GYNAECOL., KAROLINSKA HOSP., S-104 01 STOCKHOLM, SWEDEN.
SO HUM REPROD (OXF), (1988) 3 (7), 915-921.
CODEN: HUREEE. ISSN: 0268-1161.
FS BA; OLD
LA English
AB Seventeen healthy women aged 24-45 years with regular menstrual periods, proven fertility and not using steroidal **contraceptives** or IUD were recruited for the study. The volunteers were followed during one control, one treatment and one follow-up cycle. Daily morning urine samples were obtained during the control and the treatment cycle. The samples were analysed with regard to pregnanediol glucuronide (P2-G), oestrone glucuronide (E1-G), oestradiol (E2), protesterone (P4), LH and creatinine. During the entire 3-month study the subjects kept a record of uterine bleeding and side effects. The subjects received 50 mg RU486 daily either on cycle **days** 7-**10** (n = 7) or on cycle days 20-23 (n = 10). An endometrial biopsy was taken on cycle **day** **10** in the first group and on cycle **days** 21-**28** in the second group of patients. Treatment during the proliferative phase caused significant prolongation of the cycle length due to a delay of the **oestrogen** and LH surge. However, once the **oestrogen** concentration started to increase, the reamining part of the cycle was normal. The length of the follow-up cycle was similar to that of the control cycle. The morphology of the endometrium did not differ from control samples taken from untreated women at the same time of the cycle. All ovulating women (n = 9) treated in the mid-luteal phasestarted to bleed on the 3rd to 4th day of the treatment. In four of these women the bleeding was scanty and followed by a menstrual-like bleeding at expected time, while in the remaining five volunteers the treatment bleeding was heavier and not followed by a new bleeding until a month later. The duration of the secretory phase was 16.5 .+-. 1.3 days in women with two bleeding episodes and 11.8 .+-. 1.9 days in women with one bleeding episode ($P < 0.05$). The hormonal parameters were similar in both groups up to the start of the treatment. In the patients with one bleeding episode, the treatment was associated with a reduction in **progesterone** concentration, while in the patients with two bleeding episodes the **progesterone** concentration remained elevated until the second bleeding episode. Light microscopic examination of the endometrium revealed unique changes in the endometrial morphology. The results indicate that RU486 acts mainly on the endometrium but a direct or indirect effect on the corpus luteum cannot be excluded. The age of the corpus luteum may be of importance for its susceptibility to RU486 treatment.

L28 ANSWER 28 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 19
AN 1987:171658 BIOSIS
DN BA83:90099
TI A MULTI-COMPARTMENT VAGINAL RING SYSTEM FOR INDEPENDENTLY ADJUSTABLE RELEASE OF **CONTRACEPTIVE** STEROIDS.
AU DE LEEDE L G J; GOVERS C P M; DE NIJS H
CS PHARMACEUTICAL RES. AND DEVELOPMENT LAB., ORGANON INTERNATIONAL B.V., P.O. BOX 20, 5340 BH OSS, THE NETHERLANDS.

SO CONTRACEPTION, (1986 (RECD 1987)) 34 (6), 589-602.
CODEN: CCPTAY. ISSN: 0010-7824.
FS BA; OLD
LA English
AB A multi-compartment **contraceptive** vaginal ring system has been designed for the simultaneous zero-order release of **contraceptive** steroids, the rates of which can be programmed independently. This vaginal ring system consists of two or more drug-containing SilasticR tubes with an outer diameter of 5 mm. The tubes with different lengths, with a total length of 16.5 cm are connected with specially-shaped glass stoppers to obtain a ring with an outer diameter of 60 mm. The stopper prevents migration of the steroids from one compartment to the other and guarantees optimal release characteristics of both steroids even after long-term storage. An additional advantage of glass is the good adherence to SilasticR, enabling construction of systems with sufficient tensile strength. The release characteristics have been followed in vitro and can be programmed independently by changing the wall thickness of the tube (membrane thickness) and/or the length of each individual steroid-containing compartment. Multi-compartment vaginal rings were made and tested with 3-keto-**desogestrel** and ethinylestradiol. The rings had an outer diameter of 60 mm, and were fabricated with independent in vitro release rates ranging from 75 to 300 .mu.g/**day** and **10** to **30** .mu.g/**day** for, respectively, 3-keto-**desogestrel** and ethinylestradiol. Using the multi-compartment vaginal ring system, **contraceptive** devices can be fabricated relatively simply with pre-programmed release rates for a progestogen and an **estrogen** to investigate the optimal daily doses for vaginal hormonal **contraception**.

L28 ANSWER 29 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 21
AN 1984:255262 BIOSIS
DN BA77:88246
TI EFFECTS OF **CYPROTERONE ACETATE** AND ETHYNYL ESTRADIOL ON ENDOMETRIAL HISTOLOGY.
AU KLEBE U; MOLTZ L; PICKARTZ H
CS ABT. FUER GYNAEKOLOGISCHE ENDOKRINOLOGIE DER FRAUENKLINIK, KLINIKUM STEGLITZ, FREIE UNIVERSITAET BERLIN, HINDENBURGDAMM 30, D-1000 BERLIN 45, GERMANY.
SO ARCH GYNECOL, (1983 (RECD 1984)) 234 (2), 113-120.
CODEN: ARCGDG. ISSN: 0170-9925.
FS BA; OLD
LA English
AB The influence of **cyproterone acetate** (CPA) containing drugs on the endometrium has not yet been investigated. Endometrial biopsies were obtained in 22 hirsute patients between **day** **14** and **28** of the cycle after 7-18 mo. of oral antiandrogen therapy. The effects of various regimens consisting of different doses of CPA in combination with ethynylestradiol (EE) were evaluated. The low-dose standard regimen (50 .mu.g of EE plus 2 mg of CPA daily from day 5 to 25) caused regressive changes in the endometrium, i.e., sparse atrophic glands, relatively compact stroma, islands of stromal edema. These alterations correspond to those induced by conventional balanced low-dose combined oral **contraceptives**. High-dose reversed sequential regimen (40 .mu.g of EE daily from day 5-25

plus 100 mg of CPA daily from **day** 5-**14**) resulted in pseudodeciduation and massive stromal edema. Pseudodeciduation during the early secretory phase is taken as a sign of the progestational depot effect of CPA, while the stromal edema is regarded as a result of the relatively unopposed **estrogen** intake during the 2nd half of the treatment cycle. The effects of CPA-containing drug on the endometrium depend essentially on their type, dosage and and mode of administration.

L28 ANSWER 30 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 23
AN 1981:199076 BIOSIS
DN BA71:69068
TI PLASMA CYCLIC AMP DURING THE NORMAL MENSTRUAL CYCLE AND UNDER DIFFERENT HORMONAL TREATMENT.
AU GOESER R; KINDLER D; KELLER E; SCHINDLER A E
CS UNIV.-FRAUENKLIN. TUEBINGEN, D-7400 TUEBINGEN.
SO GYNECOL OBSTET INVEST, (1980 (RECD 1981)) 11 (6), 365-372.
CODEN: GOBIDS. ISSN: 0378-7346.
FS BA; OLD
LA English
AB There is a highly significant difference between the plasma cAMP values of the 1st and 2nd half of the normal menstrual cycle (**days** 1-**12**: **10**.5 .+-. 2.0 pmol, mean standard error of the mean; **days 13**-16: 21.9 .+-. 4.5; **days** 17-**28**: 19.9 .+-. 2.0; (P < 0.001). In amenorrheic patients plasma cAMP levels were nearly the same as in normal women during the first half of the menstrual cycle (11.1 .+-. 2.5). Plasma cAMP of amenorrheic women was significantly higher under human menopausal gonadotropin treatment (16.7 .+-. 2.5; P < 0.01). Under oral **contraception** with **estrogens** (alone) or with low doses of **gestagens** the plasma cAMP values were comparable to those of the amenorrheic women, but there was a dose-dependent increase of plasma cAMP under **gestagen** application. The midcyclic plasma cAMP increase is mainly caused by the gonadotropin effect, and is followed by the **progesterone** effect during the second half of the menstrual cycle. Plasma cAMP levels are in accordance to the stages of the menstrual cycle reflecting their different endocrine pattern.

L28 ANSWER 31 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1983:240289 BIOSIS
DN BA75:90289
TI ANTAGONISM OF THE ACTIONS OF **ESTROGENS** ANDROGENS AND **PROGESTERONE** BY ANORDRIN 2-ALPHA 17-ALPHA DI ETHYNYL-A NOR-5-ALPHA-ANDROSTANE-2-BETA 17-BETA-DIOL DI PROPIONATE.
AU MEHTA R R; JENCO J M; CHATTERTON R T JR; VENTON D
CS RERPRODUCTIVE ENDOCRINOLOGY LAB., DEP. OBSTETRICS AND GYNECOLOGY, NORTHWESTERN UNIV. MED. SCH., CHICAGO, IL.
SO STEROIDS, (1982) 40 (1), 65-80.
CODEN: STEDAM. ISSN: 0039-128X.
FS BA; OLD
LA English
AB Anordrin, an antifertility agent that is an antiestrogen with weak estrogenic activity, was studied to further characterize its hormonal activities. A dose of 2.0 .mu.g/mouse per day for 7 days did not increase the uterine content of protein, but it did inhibit to a small extent the effect of administered estradiol-17.beta. on uterine protein content and

more significantly the effect of estradiol-17.beta. on the uterine content of **progesterone** receptors. Anordrin also decreased serum corticosteroid-binding globulin levels. Administration of an average daily dose of 160 .mu.g/day of anordrin to intact male mice had no effect on weights of kidney, testis, or seminal vesicle after **10 days**, but seminal vesicle weight was significantly decreased after **30 days** at a slightly lower dose. Similarly, anordrin inhibited the increase in seminal vesicle weight induced by testosterone propionate treatment of castrated mice. In female mice anordrin failed to maintain deciduomata and blocked the ability of **progesterone** (2.0 mg/mouse per day) to do so. However, anordrin did not compete with the androgen [3H]R1881 [methyltrienolone] for binding in kidney cytosol or with the progestin [3H]R5020 [promegestone] for uterine receptor sites. Anordrin also did not compete with [3H]corticosterone for binding to serum proteins.

L28 ANSWER 32 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1980:289871 BIOSIS
DN BA70:82367
TI ENDOMETRIAL PATTERN IN PATIENTS WITH PRIMARY HYPO ESTROGENIC AMENORRHEA RECEIVING **ESTROGEN** REPLACEMENT THERAPY.
AU VAN CAMPENHOUT J; CHOQUETTE P; VAUCLAIR R
CS DEP. OBSTET. GYNECOL., NOTRE-DAME HOSP., 1560 E. SHERBROOKE ST., MONTREAL, QUE., CAN.
SO OBSTET GYNECOL, (1980) 56 (3), 349-355.
CODEN: OBGNAS. ISSN: 0029-7844.
FS BA; OLD
LA English
AB The association of unopposed endogenous **estrogen** secretion and endometrial carcinoma is well documented. Several recent studies have also related prolonged exogenous **estrogen** therapy and endometrial hyperplasia with carcinoma in menopausal women as well as in young women receiving sequential oral **contraceptives**. The histologic pattern of the endometrium was studied in 38 patients, 19-44 yr old, with primary hypoestrogenic amenorrhea treated by **estrogen** replacement therapy. At the time of endometrial biopsy 3 patients were receiving **estrogens** only and 35 patients were taking 1 of the following cyclic **estrogen**-progestogen combinations: conjugated **estrogens**, 1.25 or 2.5 mg/day, combined with medroxyprogesterone, 5 or 10 mg for the last 5-**10 days**; ethinyl estradiol, 50 .mu.g/day, combined with medroxyprogesterone, 5 mg/day for the last 5 **days**; or mestranol, **40** .mu.g/**day**, in combination with norethindrone, 0.5 mg for the last 7 days. Evidence of endometrial hyperplasia was found in 3 patients. Two of them were taking unopposed **estrogens** and developed cystic hyperplasia; the other patient, treated with norethindrone in addition to mestranol, disclosed focal cystic glandular hyperplasia. This study and the review of the available data reported in the literature on the endometrial response to **estrogen** therapy in patients with gonadal dysgenesis stress the importance of appropriate **estrogen** and progestogen dosage to avoid the hazards of abnormal endometrial pattern in young patients

receiving **estrogen** replacement therapy.

L28 ANSWER 33 OF 61 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1978:229387 BIOSIS
DN BA66:41884
TI EFFECT OF MEDROXY **PROGESTERONE** ACETATE **CONTRACEPTION** ON CYTOPLASMIC **ESTROGEN** RECEPTOR CONTENT OF THE HUMAN CERVIX UTERI.
AU RALL H J S; SOTO FERREIRA G; JANSSENS K Y
CS DEP. OBSTET. GYNAECOL., TYGERBERG HOSP., TYGERBERG 7505, S. AFR.
SO INT J FERTIL, (1978) 23 (1), 51-56.
CODEN: INJFA3. ISSN: 0020-725X.
FS BA; OLD
LA English
AB Specimens of cervical tissue from 5 women each on 150 mg and 450 mg regimens of medroxyprogesterone acetate (MPA) for **contraceptive** purposes were obtained through punch biopsy **15 days** after injection. In another group of 5 women each on the same **contraceptive** regimens, punch biopsies of the cervix uteri were obtained **30 days** after injection. These times corresponded to maximum and optimum blood levels of MPA, respectively. Corresponding tissue from the same anatomical position in patients matched, where possible, for age and parity was obtained from hysterectomy specimens to serve as controls. Quantification of **estrogen** receptor content in the cytoplasm of these tissues was achieved through standard procedures. MPA suppressed **estrogen** receptor content significantly compared to controls, but that there were no differences in this effect between the 2 dosages or time of biopsy.

L28 ANSWER 34 OF 61 MEDLINE DUPLICATE 22
AN 82094375 MEDLINE
DN 82094375
TI The effect of a **contraceptive** vaginal ring and oral **contraceptives** on the vaginal flora.
AU Roy S; Wilkins J; Mishell D R Jr
SO CONTRACEPTION, (1981 Oct) 24 (4) 481-91.
Journal code: DQN. ISSN: 0010-7824.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198205
AB Premenopausal women seeking a steroid **contraceptive** method were allowed to choose between a **contraceptive** vaginal ring (CVR) containing **levonorgestrel** and estradiol used in a 3-week in, 1-week out regimen (n=20) and an oral **contraceptive** (OC) containing **levonorgestrel** and ethinyl estradiol in a **28 -day** regimen (n = **10**). Cultures from the posterior vaginal fornix were obtained before therapy in both groups and monthly for 6 months for the CVR group and after 1, 3, and 6 months for the OC group. These cultures were streaked on specific media to provide quantitative aerobic and anaerobic, lactobacillus, Candida sp., Gardnerella vaginalis and Neisseria gonorrhoeae counts in micro-organisms per milliliter. A comparison of the number and types of organisms isolated from vaginal cultures obtained initially and at 6 months demonstrated no statistically

significant differences in colony counts between CVR and OC users. The results of this study suggest that the use of the CVR is not associated with a greater growth of pathogens than is oral administration of a progestin and **estrogen** combination.

L28 ANSWER 35 OF 61 MEDLINE
AN 2000104404 MEDLINE
DN 20104404
TI Endometrial histology during use of a low-dose **estrogen-desogestrel** oral **contraceptive** with a reduced hormone-free interval.
AU Archer D F
CS Jones Institute for Reproductive Medicine, Eastern Virginia Medical School, Norfolk, VA 23507-1627, USA.. archerdf@evms.edu
SO CONTRACEPTION, (1999 Sep) 60 (3) 151-4.
Journal code: DQN. ISSN: 0010-7824.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
EW 20000402
AB The object of the study was to determine the effect of a new low-dose ethinyl estradiol-**desogestrel** oral **contraceptive** on endometrial histology. The oral **contraceptive** regimen contained fixed doses of ethinyl estradiol (20 micrograms) and **desogestrel** (150 micrograms) for days 1-21, placebo on days 22 and 23, and ethinyl estradiol alone (**10** micrograms) on **days** 24-**28** . Endometrial histology was assessed in tissue samples obtained during treatment cycles 13 and 14. All endometrial samples were sent to a central laboratory for processing and evaluation. No endometrial hyperplasia or metaplasia was found in the endometrial biopsy specimens obtained during cycles 13 and 14 in a subset of 12 women participating in a multicenter efficacy and safety study. These results suggest that this oral **contraceptive** regimen, which includes 5 days of unopposed ethinyl estradiol, is not associated with endometrial hyperplasia or metaplasia. The endometrial histologic findings observed in this study were similar to those observed during the use of 21-day combination oral **contraceptive** regimens.

L28 ANSWER 36 OF 61 MEDLINE
AN 1998366399 MEDLINE
DN 98366399
TI Effects of ABT-761, a novel 5-lipoxygenase inhibitor, on the pharmacokinetics of a single dose of ethinyl estradiol and **levonorgestrel** in healthy female volunteers.
AU Wong S L; O'Dea R F; Dube L M; Awni W M
CS Abbott Laboratories, Abbott Park, Illinois 60064-3500, USA.
SO JOURNAL OF CLINICAL PHARMACOLOGY, (1998 Jul) 38 (7) 642-8.
Journal code: HT9. ISSN: 0091-2700.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 199812
EW 19981202
AB ABT-761 is a second-generation 5-lipoxygenase inhibitor in clinical development for the treatment of asthma. The effects of ABT-761 on the pharmacokinetics of an oral **contraceptive** were assessed in 21 female adult volunteers in a phase I, multiple-dose, open-label study. Subjects received a single dose of oral **contraceptive** (30 microg ethinyl estradiol and 0.15 mg of **levonorgestrel**) on each of **days** 1 and **29**. Oral doses of 300 mg of ABT-761 were administered once daily beginning on **day 15** continuing through **day 29**. Statistically significant decreases in maximum concentration (Cmax) and area under the concentration-time curve (AUC) of ethinyl estradiol were observed when oral **contraceptive** was administered concomitantly with ABT-761 compared with administration of oral **contraceptive** alone. The mean elimination rate constant of ethinyl estradiol increased by 30% (a mean decrease of 3.8 hours in half-life), and the mean apparent volume of distribution during the terminal phase (Vd(beta)/F) of ethinyl estradiol increased by 73% in the presence of ABT-761. Mean Cmax and AUC values for norgestrel decreased by 12% and 10%, respectively, when administered with ABT-761. Mean values for time to Cmax (tmax), terminal rate constant (beta), half-life (t1/2), and Vd(beta)/F of norgestrel were similar when oral **contraceptive** was administered alone or concomitantly with ABT-761. The mechanism responsible for the effect of ABT-761 on the clearance of ethinyl estradiol remains undefined. Because results of previous multiple-dose studies of ABT-761 do not provide any evidence of autoinduction, the effects of ABT-761 on the pharmacokinetics of ethinyl estradiol are more likely related to absorption of ethinyl estradiol.

L28 ANSWER 37 OF 61 MEDLINE
AN 97240880 MEDLINE
DN 97240880
TI Sequential danazol/leuprolide acetate therapy for ovarian suppression in an in vitro fertilization patient unresponsive to leuprolide acetate.
AU Balasch J; Fabregues F; Creus M; Vanrell J A
CS Department of Obstetrics and Gynecology, Faculty of Medicine, University of Barcelona, Hospital Clinic i Provincial, Spain.
SO GYNECOLOGICAL ENDOCRINOLOGY, (1997 Feb) 11 (1) 21-4.
Journal code: 125. ISSN: 0951-3590.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199707
EW 19970705
AB We report a case of pituitary-ovarian suppression obtained with sequential danazol/leuprolide acetate administration in a patient undergoing in vitro fertilization and unresponsive to leuprolide acetate alone and sequential oral **contraceptive**-leuprolide acetate therapy. Leuprolide acetate (1 mg daily subcutaneously) was administered after **5 weeks** of danazol treatment (800 mg daily) while the latter was maintained for 1 additional week. Ovarian activity was assessed by transvaginal ultrasonography and serum estradiol determination. After

5 weeks of danazol therapy, ovarian arrest was obtained despite the fact that gonadotropin serum levels did not change relative to basal values. Leuprolide acetate injection for **14 days** was associated with a decrease in serum concentrations of follicle-stimulating hormone and luteinizing hormone and a further decrease of the estradiol level. We conclude that sequential danazol/leuprolide acetate therapy is a useful alternative for obtaining ovarian arrest in patients unresponsive to leuprolide acetate alone.

L28 ANSWER 38 OF 61 MEDLINE
AN 96012363 MEDLINE
DN 96012363
TI Effect of two oral **contraceptives** containing ethinylestradiol and **gestodene** or **norgestimate** upon androgen parameters and serum binding proteins.
AU Wiegratz I; Jung-Hoffmann C; Kuhl H
CS Department of Obstetrics and Gynecology, J.W. Goethe University Frankfurt, Germany.
SO CONTRACEPTION, (1995 Jun) 51 (6) 341-6.
Journal code: DQN. ISSN: 0010-7824.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199601
AB The effect of a triphasic oral **contraceptive** containing ethinylestradiol and **gestodene** (EE/GSD) on various serum hormonal parameters was compared with that of a monophasic formulation containing 35 micrograms ethinylestradiol and 250 micrograms **norgestimate** (EE/NGM). Blood samples were collected from **46** women on **days** 2, **11**, and 21 of the preceding control cycle and of the third, sixth and twelfth treatment cycle. There was no significant difference in the influence on any hormonal parameter between both formulations. Both EE/GSD and EE/NGM caused a time-dependent suppression of serum dehydroepiandrosterone sulphate (DHEA-S) by 20-30% ($p < 0.01$) and a reduction of 5 alpha-androstane-3 alpha, 17 beta-diol glucuronide by 50-60% ($p < 0.01$) during each treatment cycle, while androstenedione levels were reduced by 25% ($p < 0.01$). There was also a significant decrease in the levels of total testosterone by 30-35% ($p < 0.01$) and free testosterone by 60% ($p < 0.01$), while sex hormone-binding globulin (SHBG) was increased by 200-240% on **days 11** and 21 ($p < 0.01$). During the pill-free interval the SHBG levels were reduced to a certain degree but remained elevated by 100% as compared to the pretreatment values. The serum levels of corticosteroid-binding globulin (CBG) which is known to be influenced only by the estrogenic component of combination pills, increased significantly by 170% ($p < 0.01$) during each treatment cycle. During the pill-free interval of 7 days, the CBG levels decreased but were still elevated by 90-100% as compared to the control cycle. Similarly, the serum levels of cortisol were significantly elevated by 110-140% ($p < 0.01$) during treatment with both preparations. The results demonstrate a

profound suppression of androgen levels and peripheral androgen metabolism.

L28 ANSWER 39 OF 61 MEDLINE
AN 92398320 MEDLINE
DN 92398320
TI Concentration of fat, protein, lactose and energy in milk of mothers using hormonal **contraceptives**.
AU Costa T H; Dorea J G
CS Department of Nutrition, Faculty of Health Sciences, University of Brasilia, Brazil..
SO ANNALS OF TROPICAL PAEDIATRICS, (1992) 12 (2) 203-9.
Journal code: 6AH. ISSN: 0272-4936.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199212
AB Energy, protein, lactose and fat were studied in the milk of mothers who were using different types of **contraceptives**. One hundred and eleven mothers made up the following groups. C: control (barrier and natural methods, or sterilization), n = 22; combined pill: LDP (low dose pill (**levonorgestrel** 0.15 mg + ethinylestradiol 0.03 mg)), n = 12 and MDP (medium dose pill (**levonorgestrel** 0.25 mg + ethinylestradiol 0.05 mg)), n = 13; MP (minipill (norethindrone 0.35 mg)), n = 37; DMPA (injectable **progesterone** (depot medroxiprogesterone acetate 150 mg)), n = 17; and IUD (plastic or copper intrauterine device), n = 10. The mean stages of lactation were, respectively, 15, 17, 5, 9, **5** and 9 **weeks**. The mean duration of observation for the study groups ranged from 2 to **4 weeks**. Milk samples were collected before and after initiation of treatment (mean = 20 **days**; range = **14**-103 **days**). The stage of lactation and the interval of nursing before sampling were recorded so that statistical account could be taken of these uncontrollable sources of variability. When incorporated as covariates, they showed that no significant differences existed between the groups tested, either before or after treatment.

L28 ANSWER 40 OF 61 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 1999279397 EMBASE
TI Psychological effects of hormone replacement therapy: A comparison of tibolone and a sequential **estrogen** therapy.
AU Ross L.A.; Alder E.M.; Cawood E.H.H.; Brown J.; Gebbie A.E.
CS Dr. E.M. Alder, Dept. Epidemiology and Public Health, University of Dundee, Ninewells Hospital Medical School, Dundee DD1 9SY, United Kingdom
SO Journal of Psychosomatic Obstetrics and Gynaecology, (1999) 20/2 (88-96).
Refs: 23
ISSN: 0167-482X CODEN: JPOGDP
CY United Kingdom
DT Journal; Article
FS 010 Obstetrics and Gynecology
032 Psychiatry
037 Drug Literature Index

LA English
SL English
AB Hormone replacement therapy (HRT) is effective in alleviating vasomotor symptoms but the effect on psychological symptoms is less clear. This study aimed to compare the psychological effects of two regimens of HRT in perimenopausal women in a randomized, initially double-blind, controlled trial. Thirty-eight women reporting climacteric symptoms were randomly allocated into either oral conjugated equine **estrogen** 0.625 mg daily plus progestogen (norgestrel) 150 .mu.g for the last **12 days** of each **28 day** cycle, or tibolone 2.5 mg/**day** for **28 days**. They were assessed using standardized psychological assessments. There were no significant differences in changes from baseline between the two types of therapy. For both groups combined there were significant improvements compared with baseline in vasomotor symptoms in the first month, plus anxiety, sleep, memory and somatic dysfunction by the second and third months, but not in scores of depression. Log linear analysis of weekly scores showed that depression scores were significantly related to improvement in vasomotor scores independent of type of therapy and time on HRT. Memory problems were related to vasomotor symptoms independent of depression. No difference between the two types of therapy was found, nor any direct effect of HRT on anxiety or depression. The results support the domino theory, suggesting that psychological improvement follows alleviation of vasomotor symptoms.

L28 ANSWER 41 OF 61 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 95310832 EMBASE
DN 1995310832
TI Lifetime alcohol consumption and breast cancer risk among postmenopausal women in Los Angeles.
AU Longnecker M.P.; Paganini-Hill A.; Ross R.K.
CS Epidemiology Branch, NIEHS, P.O. Box 12233,Research Triangle Park, NC 27709, United States
SO Cancer Epidemiology Biomarkers and Prevention, (1995) 4/7 (721-726). ISSN: 1055-9965 CODEN: CEBPE4
CY United States
DT Journal; Article
FS 016 Cancer
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LA English
SL English
AB Although most data support an overall relation of alcohol consumption with risk of breast cancer, the timing of alcohol consumption as it relates to risk of breast cancer is still debatable. The authors examined this issue in a case-control study conducted among non-Hispanic white and Hispanic women in Los Angeles. Cases aged 55-64 years at diagnosis in 1987-1989 were enrolled through the Cancer Surveillance Program of Los Angeles County (a Surveillance, Epidemiology, and End Results Program registry). Community controls were individually matched to cases by age (.+-. 3 years), ethnicity, and neighborhood. In-person interviews were completed with 1510 matched pairs, of which 1431 met the inclusion criteria for the present analysis. In a multivariate conditional logistic regression model that simultaneously included terms for alcohol consumption at age 25

years, age 40 years, and in the recent past, clear differences among the age-specific associations were not observed, and the results suggested that intake at each time independently contributed to risk. The odds ratios associated with estimated average lifetime intake were: for <6 g/day, 1.01; for 6-**11** g/**day**, 1.21; for **12**-18 g/**day**, 0.94; for 19-**32** g/**day**, 1.63; for **33-45** g/**day**, 2.45 and for .gtoreq. **46** g/**day**, 0.94 compared with abstainers (P for trend = 0.01). Use of **estrogen** replacement therapy did not modify the risk associated with alcohol consumption, in contrast with the findings in two previous studies. This large study supports a relation between risk of breast cancer and alcohol consumption and suggests that lifetime intake may be the best indicator of alcohol-associated risk.

L28 ANSWER 42 OF 61 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 94089165 EMBASE
DN 1994089165
TI Changes in mammographic densities induced by a hormonal **contraceptive** designed to reduce breast cancer risk.
AU Spicer D.V.; Ursin G.; Parisky Y.R.; Pearce J.G.; Shoupe D.; Pike A.; Pike M.C.
CS Univ. Southern California Med. Sch., 1420 San Pablo St.,Los Angeles, CA 90033-9987, United States
SO Journal of the National Cancer Institute, (1994) 86/6 (431-436). ISSN: 0027-8874 CODEN: JNCIAM
CY United States
DT Journal; Article
FS 014 Radiology
016 Cancer
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Background: It has been known for some time that oral **contraceptives** substantially reduce the risk of endometrial and ovarian cancer, but they do not reduce the risk of breast cancer. A hormonal **contraceptive** regimen has been developed which uses a gonadotropin-releasing hormone agonist (GnRHA) to suppress ovarian function, and this regimen includes the administration of very low doses of both **estrogen** and progestogen. This hormonal **contraceptive** regimen attempts to minimize exposure of the breast epithelium to these steroids and to preserve the maximum beneficial effects of **estrogen**, while still preventing endometrial hyperplasia. Purpose: Our purpose was to determine whether changes occurred in mammographic densities between baseline and 1 year for women on this hormonal **contraceptive** regimen with reduced **estrogen** and progestogen levels compared with women in a control group. Methods: Twenty-one women were randomly assigned in a 2:1 ratio to the GnRHA- based **contraceptive** group (14 women) or to a control group (seven women). The **contraceptive** group received the following: 7.5 mg leuprolide acetate depot by intramuscular injection every **28 days**; 0.625 mg conjugated **estrogen** by mouth for 6 days out of 7 every week; and 10 mg medroxy-**progesterone** acetate orally for **13 days** every fourth **28-day** cycle. The control group received no medication. Baseline and 1-year follow-up mammograms of

contraceptive and control subjects were reviewed in a blinded fashion by two radiologists. Results: Comparison of the changes between the baseline and 1-year mammograms in the two groups of women showed significant (P = .039) reduction in mammographic densities at 1 year for women on the **contraceptive** regimen. Assessing the reduction in mammographic densities by noting the fineness of fibrous septae showed a highly significant (P = .0048) difference in the **contraceptive** regimen group. One of the women on the **contraceptive** regimen was withdrawn from the study because of poor compliance. Conclusion: The reduced **estrogen** and progestogen exposures to the breast that were achieved by the hormonal **contraceptive** regimen resulted in substantial reductions in follow-up mammographic densities at 1 year compared with baseline. Although there is no direct evidence that such a reduction in densities will lead to a reduced risk of breast cancer, indirect evidence for a protective effect of this regimen is that early menopause reduces breast cancer risk, and that menopause is associated with a reduction in mammographic densities.

L28 ANSWER 43 OF 61 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 89187805 EMBASE
DN 1989187805
TI LHRH agonists and the prevention of breast and ovarian cancer.
AU Pike M.C.; Ross R.K.; Lobo R.A.; Key T.J.A.; Potts M.; Henderson B.E.
CS Department of Preventive Medicine, University of Southern California Medical School, Los Angeles, CA 90033, United States
SO British Journal of Cancer, (1989) 60/1 (142-148).
ISSN: 0007-0920 CODEN: BJCAAI
CY United Kingdom
DT Journal
FS 010 Obstetrics and Gynecology
016 Cancer
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LA English
SL English
AB Early age at natural menopause or bilateral ovariectomy substantially reduce a woman's lifetime risk of breast cancer. Reversible 'bilateral ovariectomy' can now in effect be achieved by 'high-dose' luteinizing hormone releasing hormone (LHRH) agonists (LHRHAs). The harmful effects of such medical reversible bilateral ovariectomy, in particular the increased risks of corornary heart disease and osteoporosis, can in all likelihood be obviated by 'low-dose' **oestrogen** replacement therapy (ERT), specifically 0.625 mg of conjugated equine **oestrogens** (CEE) for 21 **days** in each **28-day** treatment cycle, and such ERT use will only negate to a relatively small extent the beneficial effect of such bilateral ovariectomy on breast cancer risk. We calculate that such a LHRHA plus low-dose ERT regimen given to a premenopausal woman for 10 years will, in addition to being a most effective **contraceptive**, decrease her lifetime risk of breast cancer by more than 50%. We calculate that such a 10-year regimen will also decrease her risk of ovarian cancer by two-thirds. This regiman should leave endometrial cancer risk and bone metabolism unaltered, and may reduce the risk of heart disease. The addition of a 'low-dose' progestogen to the regimen for **12 days** in each **28-day**

treatment cycle would be beneficial to the endometrium, but it will adversely affect risk factors for heart disease and it may significantly reduce the benefit of the regimen as regards breast cancer. A satisfactory compromise may be to add a low-dose progestogen for **12 days** at less frequent intervals. Another possibility may be to deliver a progestogen solely to the endometrium with an intra-uterine device; the benefits of such a regimen would be a significant reduction in the incidence of breast, ovarian and endometrial cancer.

L28 ANSWER 44 OF 61 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 89079167 EMBASE
DN 1989079167
TI Effects of oral **contraceptive** and **estrogen** administration on plasma calcitonin in pre- and postmenopausal women.
AU Hurley D.L.; Tiegs R.D.; Barta J.; Laakso K.; Heath III H.
CS Endocrine Research Unit, Division of Endocrinology and Metabolism, Department of Medicine, Mayo Clinic, Rochester, MN 55905, United States
SO Journal of Bone and Mineral Research, (1989) 4/1 (89-95).
ISSN: 0884-0431 CODEN: JBMREJ
CY United States
DT Journal
FS 003 Endocrinology
006 Internal Medicine
010 Obstetrics and Gynecology
020 Gerontology and Geriatrics
037 Drug Literature Index
LA English
SL English
AB **Estrogen** (E) therapy and administration of oral **contraceptives** (OC) reportedly increase plasma calcitonin (CT) concentrations in women, effects said to mediate in part the beneficial actions of E on bone. To further examine this theory, we tested the effects of three cycles of OC therapy in 12 young women, comparing them to 10 healthy women before and after three normal menstrual cycles. We also determined the effects of 3 months of E therapy (ethinyl estradiol, 20 .mu.g/**day**, 25 of **30 days**) in **14** healthy postmenopausal women, using a crossover design (studied after 3 months with and 3 months without E). We determined CT by radioimmunoassay (antiserum G-1701) in whole plasma (iCT) and silica cartridge extracts of plasma (exCT) after overnight fasting, after calcium (Ca) infusion (2 mg Ca/kg over 5 minutes), and during a normal day at 0800, 1200, 1700, and 2000 h. In no control study was there a significant diurnal change in iCT or exCT, and neither OC nor E therapy altered this. Similarly, OC administration did not affect basal CT levels or the normal iCT and exCT responses to Ca infusion. E therapy induced expected changes in serum Ca, phosphorus, and alkaline phosphatase and urinary Ca and cAMP excretion; basal and diurnal plasma exCT levels were decreased significantly, consonant with the decrement in serum Ca. E did not alter normal iCT and exCT responses to Ca infusion. Thus, administration of either OC or E has no stimulatory effect on CT secretion, which suggests that the beneficial actions of E on bone are not mediated through CT-induced inhibition of bone resorption. Interaction of E with CT action at the cellular level is not excluded by these findings, but there are no data to support such proposal.

Searched by John Dantzman 308-4488

L28 ANSWER 45 OF 61 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 79171472 EMBASE
DN 1979171472
TI The vitamin B6 requirement in oral **contraceptive** users. I. Assessment by pyridoxal level and transferase activity in erythrocytes.
AU Bosse T.R.; Donald E.A.
CS Fac. Home Econ., Univ. Alberta, Edmonton T6G 2M8, Canada
SO American Journal of Clinical Nutrition, (1979) 32/5 (1015-1023). CODEN: AJCNAC
CY United States
DT Journal
FS 037 Drug Literature Index
017 Public Health, Social Medicine and Epidemiology
003 Endocrinology
025 Hematology
LA English
AB 8 College-age women using **estrogen**-containing oral **contraceptives** (OC) were fed a low vitamin B6 diet (0.36 mg/**day**) for **42 days**. During the first **10 days** (adjustment period) the diet was supplemented with 1.7 mg pyridoxine hydrochloride bringing the total intake to 2.06 mg/day. Following depletion, repletion was done in three consecutive steps: intakes of 0.96, 1.56, and 5.06 mg were consumed for 8, 9, and 7 days, respectively. Continuous 24-hr urine collections were made throughout the study and fasting blood samples were drawn periodically. Vitamin B6 nutriture was assessed by erythrocyte pyridoxal level, erythrocyte alanine aminotransferase and erythrocyte aspartic aminotransferase activity; and stimulation of these enzyme systems with pyridoxal phosphate. Results were compared with data obtained from non-OC users who consumed a similar diet. The data obtained suggest that 0.96 mg vitamin B6 was not adequate to meet the needs of OC users. Predepletion levels had been reached in almost all subjects at an intake of 1.5 mg/day. Assessed by the parameters studied, an intake between 1.5 and 5.0 mg/day of vitamin B6 was adequate to meet the needs of OC users; this compares with 1.5 mg/day previously suggested for the nonuser.

L28 ANSWER 46 OF 61 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 77144459 EMBASE
DN 1977144459
TI Action of a midcycle **contraceptive** (R 2323) on the human endometrium.
AU Azadian Boulanger G.; Secchi J.; Laraque F.; et al.
CS Cent. Rech. Roussel Uclaf, Romainville, France
SO American Journal of Obstetrics and Gynecology, (1976) 125/8 (1049-1056). CODEN: AJOGAH
DT Journal
FS 037 Drug Literature Index
010 Obstetrics and Gynecology
030 Pharmacology
LA English
AB Over 2,148 cycles of midcycle oral administration of R 2323 (50 mg. per **day** on **days 15**, 16, and 17), the authors

recorded a drug failure pregnancy rate of 5% and an unusually regular cycle length of **28** .+-. 2 **days**. During this trial, endometrial biopsies obtained in the luteal phase were examined by light and electron microscopy and compared to pretreatment biopsies. Light microscopy indicated a weakly secretory endometrium suggestive of some, albeit low, **progesterone** impregnation. Ultrastructural examination revealed deleterious changes in the development of the nucleolar channel system and giant mitochondria and a delay in the migration of glycogen granules. This low **progesterone** impregnation could be explained either by a direct effect of R 2323 on cell ultrastructure or by interference with **progesterone** availability. It would appear that R 2323 acts as a temporary substitute for **progesterone** at the receptor level but that it does not induce all the biological manifestations of this hormone, in particular, the endometrial changes required for implantation.

L28 ANSWER 47 OF 61 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 75145982 EMBASE
DN 1975145982
TI A new approach to **estrogen** free **contraception** based on **progesterone** receptor blockage by mid cycle administration of ethyl norgestrienone (R 2323).
AU Sakiz E.; Azadian Boulanger G.; Laraque F.; Raynaud J.P.
CS Cent. Rech. Roussel Uclaf, Romainville, France
SO Contraception, (1974) 10/5 (467-474).
CODEN: CCPTAY
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
030 Pharmacology
010 Obstetrics and Gynecology
LA English
AB Attempts to prevent conception without ovulation inhibition have failed so far. The daily use of progestins interferes with the hormonal pattern and disrupts the cycle. Since the antiprogesterone, 13-ethyl 17-hydroxy 18, 19-dinor 17.alpha.-pregna 4,9,11-trien 20-yn 3-one (R 2323), competes for the **progesterone**/progestin binding sites of the uterine cytosol receptor in various species, it was postulated that blockage by R 2323 of **progesterone** binding to the **estrogen** induced receptor at the beginning of the luteal phase could upset **progesterone** dependent changes and thus exert a **contraceptive** effect. In a 2 yr clinical trial in Haiti (1362 cycles), R 2323 (50 mg) has been administered orally, once a day for 3 consecutive days, exactly 2 wk after the first day of menstrual bleeding (**15**, 16, 17th **days**). Results indicate that: cycle length varies from 21 to **35** **days** (93%), but is perfectly regular for each woman; there is no incidence of amenorrhea, menstrual bleeding lasts 3 to 5 days (83%) with hardly any spotting or breakthrough bleeding (9%). The main side effect is vomiting. Pregnancy rate expressed as the Pearl Index is 4.6% for drug failure and 5.5% for patient failure. Since 4 pregnancies are due to omissions, it appears that R 2323 does not affect return to fertility.

L28 ANSWER 48 OF 61 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 1999:79881 SCISEARCH

GA The Genuine Article (R) Number: 157MD
TI Prospective randomized study comparing the long-acting gonadotropin-releasing hormone agonist triptorelin, flutamide, and **cyproterone acetate**, used in combination with an oral **contraceptive**, in the treatment of hirsutism
AU Pazos F; EscobarMorreale H F; Balsa J; Sancho J M; Varela C (Reprint)
CS HOSP RAMON Y CAJAL, DEPT ENDOCRINOL, CARRETERA COLMENAR KM 9-100, MADRID 28034, SPAIN (Reprint); HOSP RAMON Y CAJAL, DEPT ENDOCRINOL, MADRID 28034, SPAIN
CYA SPAIN
SO FERTILITY AND STERILITY, (JAN 1999) Vol. 71, No. 1, pp. 122-128. Publisher: AMER SOC REPRODUCTIVE MEDICINE, 1209 MONTGOMERY HIGHWAY, BIRMINGHAM, AL 35216-2809. ISSN: 0015-0282.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 33
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Objective: To compare triptorelin, **cyproterone acetate** (CPA), and flutamide, in combination with an oral **contraceptive**, in the treatment of hirsutism.

Design: Prospective randomized study. Setting(s): Tertiary care hospital.

Patient(s): Thirty-nine hirsute women with idiopathic or functional ovarian hyperandrogenism.

Intervention(s): Patients were randomly assigned to receive triptorelin (3.75 mg IM every **28 days**), CPA (100 mg/d orally on **days 1-10** of the menstrual cycle), or flutamide (250 mg orally twice daily). All the patients also received a triphasic oral **contraceptive**.

Main Outcome Measure(s): Before and after 3 and 9 months of treatment, the Ferriman-Gallwey score, hepatic function, and gonadal and adrenal steroid profiles were evaluated.

Results: Thirty-three patients completed the 9-month study period. The Ferriman-Gallwey score decreased in all the groups. In the patients treated with CPA or flutamide, a decrease in the hirsutism score was noted as soon as after 3 months of treatment. This decrease was more pronounced after 9 months of treatment, especially in the patients who received flutamide, who had lower hirsutism scores compared with the other treatment groups. None of the patients had abnormal liver function test results. There was a mild increase in serum lipid concentrations, mostly in the group treated with triptorelin.

Conclusion(s): Triptorelin, CPA, and flutamide are effective drugs for thr treatment of hirsutism. Flutamide results in a greater reduction in the hirsutism score, but CPA also offers satisfactory results at a much lower cost. Triptorelin has no advantages over flutamide and CPA, and is the most expensive of the three drugs tested. (C) 1998 by American Society for Reproductive Medicine.

L28 ANSWER 49 OF 61 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 1998:752730 SCISEARCH
GA The Genuine Article (R) Number: 123DK

TI The influence of female sexhormones on skin thickness: evaluation using 20
MHz sonography
AU Eisenbeiss C (Reprint); Welzel J; Schmeller W
CS UNIV LUBECK, DEPT DERMATOL, RATZEBURGER ALLEE 160, D-23538 LUBECK, GERMANY
(Reprint)
CYA GERMANY
SO BRITISH JOURNAL OF DERMATOLOGY, (SEP 1998) Vol. 139, No. 3, pp. 462-467.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0007-0963.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 22
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Changes in skin thickness and echodensity during the spontaneous menstrual cycle, in women taking hormonal **contraceptives** and pregnant women were investigated by high-frequency (20 MHz) ultrasound. Women with a spontaneous ovulatory menstrual cycle (group I), women taking one-phase **contraceptives** (group IT), women taking three-phase **contraceptives** (group III) and pregnant women (group IV) were measured at the following locations: proximal and distal forearm and lower leg on both sides. The skin was investigated during three phases of the menstrual cycle: days 2-4 (phase A), **days 12-14** (phase B) and days 20-22 (phase C). Oestradiol and **progesterone** levels were determined at each phase. The pregnant women were investigated 2 **weeks** prepartal and **6 weeks** after delivery Group I showed a statistically significant increase in the skin thickness from phase A to phase B, but not from phase B to phase C. Group II showed no significant changes in skin thickness, whereas the skin thickness increased from phase A to phase B in group III. In group IV, the skin was significantly thicker prepartal than after delivery. The measured echodensity showed a negative correlation with skin thickness in group III and in pregnant women. We were able to demonstrate that the status of female sex hormones influences the thickness of the skin. These results can be explained by hormone-induced water retention in the skin. Sonography at 20 MHz is able to quantify these effects, which should be considered when performing ultrasound measurement in women.

L28 ANSWER 50 OF 61 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 96:240863 SCISEARCH
GA The Genuine Article (R) Number: UA868
TI VENTILATORY AND BLOOD LACTATE RESPONSES TO MAXIMAL TREADMILL EXERCISE DURING THE MENSTRUAL-CYCLE
AU BEMBEN D A (Reprint); SALM P C; SALM A J
CS UNIV OKLAHOMA, HLTH SCI CTR, HUSTON HUFFMAN CTR, DEPT HLTH & SPORT SCI, ROOM 120, 1401 ASP AVE, NORMAN, OK, 73019 (Reprint); NE MISSOURI STATE UNIV, DIV HLTH & EXERCISE SCI, KIRKSVILLE, MO, 63501; VALPARAISO UNIV, DEPT PHYS EDUC, VALPARAISO, IN, 46383; PORTER MEM HOSP, VALPARAISO, IN,

00000
CYA USA
SO JOURNAL OF SPORTS MEDICINE AND PHYSICAL FITNESS, (DEC 1995) Vol. 35, No. 4, pp. 257-262.
ISSN: 0022-4707.
DT Article; Journal
FS CLIN
LA ENGLISH
REC Reference Count: 22
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB This investigation examined ventilatory and blood lactate responses to maximal treadmill exercise during the early follicular (EF), late follicular (LF), and mid-luteal (ML) phases of the menstrual cycle, Subjects were moderately active women (n=5), 20-24 years of age with regular menstrual cycles 25-**36 days** in length, Menstrual cycle phase (EF days 2-5; LF **days** 12-**15**; ML **days** 20-23) was verified by basal body temperatures and serum **progesterone** levels, Each subject performed a progressive incremental treadmill test to max during EF, LF and ML. Metabolic and ventilatory variables and heart rate were measured continuously during the tests, Ventilatory Threshold (VT) was estimated from ventilatory parameters (V-E-VO2 and VCO2-VO2 curves), Venous blood samples were withdrawn 5 min prior to exercise and 3 min post-exercise for hematocrit, lactate and **progesterone** analyses, Body weight and plasma volume changes were not different (p>0.05) between the phases, Additionally, VO2 max, V-E max, VCO2 max, post-exercise blood lactate and time to exhaustion were similar (p<0.05) during the menstrual cycle, Relative VT occurred at a significantly higher (p=0.02) percentage of VO2 max in EF compared to ML, and approached significance (p=0.06) for EF compared to LF. We concluded that, with the exception of relative VT, metabolic and performance variables measured during maximal treadmill exercise were not dependent on menstrual cycle phase.

L28 ANSWER 51 OF 61 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 95:109317 SCISEARCH
GA The Genuine Article (R) Number: QD584
TI THE PROLIFERATION OF NORMAL HUMAN BREAST-TISSUE IMPLANTED INTO ATHYMIC NUDE-MICE IS STIMULATED BY **ESTROGEN** BUT NOT **PROGESTERONE**
AU LAIDLAW I J; CLARKE R B; HOWELL A; OWEN A W M C; POTTEN C S; ANDERSON E (Reprint)
CS CHRISTIE HOSP NATL HLTH SERV TRUST, DEPT CLIN RES, TUMOUR BIOCHEM LAB, WILMSLOW RD, MANCHESTER M20 9BX, LANCS, ENGLAND (Reprint); CHRISTIE HOSP NATL HLTH SERV TRUST, DEPT CLIN RES, TUMOUR BIOCHEM LAB, MANCHESTER M20 9BX, LANCS, ENGLAND; CHRISTIE HOSP NATL HLTH SERV TRUST, CRC, DEPT MED ONCOL, MANCHESTER M20 9BX, LANCS, ENGLAND; UNIV S MANCHESTER HOSP, DEPT SURG, MANCHESTER M20 8LR, LANCS, ENGLAND; PATERSON INST CANC RES, DEPT EPITHELIAL BIOL, MANCHESTER M20 9BX, LANCS, ENGLAND
CYA ENGLAND
SO ENDOCRINOLOGY, (JAN 1995) Vol. 136, No. 1, pp. 164-171.
ISSN: 0013-7227.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In order to resolve the question of which ovarian steroid stimulates

normal human mammary epithelial cell proliferation, we have implanted pieces of normal human breast tissue subcutaneously into athymic nude mice. These mice were then treated with slow-release pellets containing estradiol (E(2)) or **progesterone** (P) such that serum levels of E(2) and P were increased to those seen in normal women. The proliferative activity of the tissue implants was assessed by uptake of tritiated thymidine and steroid receptor expression was measured immunocytochemically.

Insertion of a 2 mg E(2) pellet **14 days** after tissue implantation increased the thymidine labeling index (TLI) from a median of 0.4% (n = 34) to a median of 2.1% after 7 **days** (n = **43**; P < 0.001 by Mann Whitney U test). In contrast, treatment with a P pellet (4 mg) had no effect upon the TLI whereas P (4 mg) in combination with E(2) (2 mg) had no effect over and above that of E(2) alone. There was a significant correlation between the increase in TLI and either the E(2) content of the pellets (P < 0.001 by linear regression) or the serum E(2) levels achieved (P < 0.001). Expression of the P receptor was increased 15- to 20-fold by E(2) treatment.

We conclude that E(2) is sufficient to stimulate human breast epithelial cell proliferation at physiologically relevant concentrations and that P does not affect proliferation either alone or after E(2) priming.

L28 ANSWER 52 OF 61 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 93:655240 SCISEARCH
GA The Genuine Article (R) Number: MD237
TI EFFECT OF **NORETHISTERONE** AND **LEVONORGESTREL** IN LOW-DOSE MULTIPHASIC ORAL-**CONTRACEPTIVES** ON SERUM-LIPIDS
AU WIIK P (Reprint); NORDBY J; PAULSEN J E
CS SKEDSMO HELSESTASJUN UNGDOM, LILLESTROM, NORWAY; SYNTEX NORWAY, STROMMEN, NORWAY
CYA NORWAY
SO ACTA OBSTETRICIA ET GYNECOLOGICA SCANDINAVICA, (OCT 1993) Vol. 72, No. 7, pp. 550-555.
ISSN: 0001-6349.
DT Article; Journal
FS CLIN
LA ENGLISH
REC Reference Count: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In a parallel, multicenter study in Norway and Finland involving a total of 196 healthy women (mean age 22.4 years, range 18-30), the effects on serum lipids and lipoproteins of two multiphasic oral **contraceptives** containing ethinyl estradiol (EE) but different progestins were examined. One formulation contained EE 35 mug and **norethisterone** (NET) 0.5 mg on days 1-7 and days 17-21 and elevated NET 1.0 mg during the midphase (days 8-16). The other formulation contained EE **30** mug on **days** 1-6 and **days** **12**-21 and **40** mug on **days** 7-**11** and phased **levonorgestrel** (LGN): 50 mug (days 1-6), 75 mug (**days** 7-**11**) and 125 mug (**days** **12**-21).
Both formulations induced significant elevation of total cholesterol (6.7

and 4.1%), Apo B (8.1 and 7.0%) as well as HDL (6.4 and 3.7%) for the EE/NET and EE/LGN formulation respectively. Mean serum levels of triglycerides were significantly elevated (58 and 47%). However, all mean serum lipid and lipoprotein values remained within the normal range, and no change in the calculated cholesterol ratio (HDL/total cholesterol) nor lipoprotein ratio (HDL/(HDL + LDL)) was observed. No significant difference between the formulations could be detected with respect to the effect on serum lipids and lipoproteins measured. The change in total cholesterol was smaller than reported in many studies of monophasic preparations. Taken together, these data suggest that only small alterations in lipid metabolism are elicited by these oral **contraceptives**.

L28 ANSWER 53 OF 61 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 91:434083 SCISEARCH
GA The Genuine Article (R) Number: FY511
TI COMPARISON OF TRANSDERMAL TO ORAL ESTRADIOL ADMINISTRATION ON HORMONAL AND
HEPATIC PARAMETERS IN WOMEN WITH PREMATURE OVARIAN FAILURE
AU STEINGOLD K A (Reprint); MATT D W; DEZIEGLER D; SEALEY J E; FRATKIN M; REZNIKOV S
CS VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, DEPT OBSTET & GYNECOL, RICHMOND, VA, 23298 (Reprint); VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, DEPT MED, RICHMOND, VA, 23298; UNIV MED & DENT NEW JERSEY, NEW JERSEY MED SCH, DEPT OBSTET & GYNECOL, NEWARK, NJ, 07103; CORNELL UNIV, MED CTR, NEW YORK HOSP, DEPT MED, NEW YORK, NY, 10021
CYA USA
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1991) Vol. 73, No. 2, pp. 275-280.
DT Article; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Five women with premature ovarian failure were studied in a randomized cross-over design to compare the biochemical effects of transdermal to oral estradiol administration when used in doses appropriate for endometrial preparation in a donor oocyte program. Patients randomly received increasing dosages of oral micronized or transdermal estradiol for **4 weeks**, with **progesterone** added in the last 2 weeks, to mimic a normal hormonal cycle. Serum samples were assayed throughout treatment and compared to those from normally cycling premenopausal controls.

In general, serum estradiol remained within the normal range in both treatment groups, whereas peak serum estrone levels were 10-fold higher in the orally treated group than those in the transdermally treated group. Serum levels of sex hormone-binding globulin, thyroid binding globulin, and renin substrate were all significantly elevated by **day 14** in the orally treated patients and unchanged in the transdermal subjects. While plasminogen was unaltered by either route of administration, antithrombin-III levels fell with both treatments. Changes in gonadotropin levels were similar in both groups, with suppression of FSH by the end of the simulated cycles, but not into the normal premenopausal range.

Searched by John Dantzman 308-4488

In conclusion, both **estrogen** replacement regimens provided near-normal serum estradiol profiles. However, despite the relatively high doses necessary to mimic a hormonally normal cycle, the transdermal route did not significantly alter the hepatic parameters studied, suggesting that this route of administration may have less adverse hepatic effects.

L28 ANSWER 54 OF 61 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-243168 [20] WPIDS
DNC C1999-070799
TI **Contraception** method comprising oral administration of a biphasic combination of progestin and **estrogen**.
DC B01 B07
IN GAST, M J
PA (AMHP) AMERICAN HOME PROD CORP
CYC 1
PI US 5888543 A 19990330 (199920)* 6p
ADT US 5888543 A Provisional US 1996-22681 19960726, US 1997-886070 19970702
PRAI US 1996-22681 19960726; US 1997-886070 19970702
AN 1999-243168 [20] WPIDS
AB US 5888543 A UPAB: 19990525
NOVELTY - A **contraception** method comprises oral administration of a biphasic combination of progestin/**estrogen**, with reduced total **contraceptive** steroid administration (particularly **estrogen**) per **28-day** cycle.

DETAILED DESCRIPTION - A **contraception** method comprises orally administering to a female of child-bearing age, for 23-25 consecutive **days** of a **28-day** menstrual cycle:

(a) a first phase combination of

(i) a progestin at a daily dosage of 40-500 micro g trimegastone or 250 micro g-4 mg **dienogest**; and

(ii) an **estrogen** at a daily dosage equivalent in activity to 10-20 micro g ethinyl estradiol; for 9-**13 days** beginning on day 1 of the menstrual cycle, where the same dosage of the progestin and **estrogen** combination is administered on each day; and

(b) a second phase combination of

(i) a progestin at a daily dosage of 40-250 micro g trimegastone or 400 micro g-4 mg **dienogest**; and

(ii) an **estrogen** at a daily dosage equivalent in activity to 10-20 micro g ethinyl estradiol; for **11-15 days** beginning on the day immediately following the last day of administration of the first phase combination, where the same dosage of the progestin and **estrogen** combination is administered on each day; provided that the daily dosage of second phase progestin is greater than the daily dosage of the first phase progestin, and the daily dosage of the second phase **estrogen** is greater than or equal to the daily dosage of the first phase **estrogen**;

provided that no oral **contraceptives** are administered for the remainder of the **28 day** menstrual cycle following the 23-25 day administration.

INDEPENDENT CLAIMS are included for:

(1) a **contraceptive** kit for daily oral administration comprising:

(a) 9-13 first phase dosage units;

(b) and 11-15 second phase dosage units, with a total of 23-25 dosage

units; and
(2) a **contraceptive** kit for daily oral administration comprising:
(a) 9-13 first phase and 11-15 second phase dosage units, and
(b) 11-15 second phase dosage units, and 3-5 dosage units each containing a non **contraceptive** placebo, so that the total number of dosage units is 28.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - For **contraceptive** use. Following the 23-25 day administration period, a non-**contraceptive** placebo may be administered so that the total administration period is **28 days**, to aid in compliance.
ADVANTAGE - There are minimal side effects, with reduced total **contraceptive** steroid administration compared with other methods.
Dwg.0/0

L28 ANSWER 55 OF 61 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-178953 [16] WPIDS
DNC C1998-057406
TI Improved method of **contraception** requiring reduced amounts of steroid - comprises treatment phases using combinations of an **oestrogen** and a progestin.
DC B01 B07
IN GAST, M J
PA (AMHP) AMERICAN HOME PROD CORP
CYC 78
PI WO 9804268 A1 19980205 (199816)* EN 26p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9738076 A 19980220 (199828)
EP 917466 A1 19990526 (199925) EN
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE SI
BR 9710565 A 19990817 (199954)
CN 1230888 A 19991006 (200006)
AU 713016 B 19991118 (200007)
ADT WO 9804268 A1 WO 1997-US12786 19970723; AU 9738076 A AU 1997-38076 19970723; EP 917466 A1 EP 1997-935047 19970723, WO 1997-US12786 19970723; BR 9710565 A BR 1997-10565 19970723, WO 1997-US12786 19970723; CN 1230888 A CN 1997-198093 19970723; AU 713016 B AU 1997-38076 19970723
FDT AU 9738076 A Based on WO 9804268; EP 917466 A1 Based on WO 9804268; BR 9710565 A Based on WO 9804268; AU 713016 B Previous Publ. AU 9738076, Based on WO 9804268
PRAI US 1996-686786 19960726
AN 1998-178953 [16] WPIDS
AB WO 9804268 A UPAB: 19980421
Method of **contraception** comprises administering to females of child bearing age for 23-25 consecutive days: (a) a first phase combination of a progestin (comprising 40-500 mu g trimegestrone (I), 250 mu g - 4 mg **dienogest** (II) and 250 mu g - 4 mg **drospirenone** (III)) and an **oestrogen** at a dosage equivalent in oestrogenic activity to 10-20 mu g ethinyl oestradiol (EO) for 3-8 days, beginning on day 1 of the menstrual cycle, the same dosage

being administered each day; (b) a second combination of a progestin comprising 40-500 mu g (I), 250 mu g - 4 mg (II) and 250 mu g - 4 mg (III)) and an **oestrogen** at a dosage equivalent in oestrogenic activity to comprising 10-20 mu g EO for 4-**15 days** beginning on the day immediately following the last day of administration of the first phase combination, the same dosage being administered each day; (c) a third phase combination of a progestin comprising 40-500 mu g (I), 250 mu g - 4 mg (II) and 250 mu g - 4 mg (III)) and an **oestrogen** at a dosage equivalent in oestrogenic activity to 10-20 mu g EO for 4-**15 days** beginning on the day immediately following the last day of administration of the second phase combination, the same dosage being administered each day; provided that the daily dosage of the combination administered in the first phase is not the same as the daily dosage of the combination administered in the second phase and that the daily dosage of the combination administered in the second phase is not the same as that administered in the third phase. Also claimed are: (A) a three-phase **contraceptive** kit adapted for daily oral administration of the above phases comprising 3-8 first phase dosage units, 4-15 second phase dosage units and 4-15 third phase dosage units, the total number of dosage units being 23-25; and (B) a **contraceptive** kit adapted for daily oral administration of the above phases comprising 3-8 first phase dosage units, 4-15 second phase dosage units, 4-15 third phase dosage units and 3-5 non-**contraceptive** placebo dosage units, the total number of dosage units being 28.

ADVANTAGE - The method provides effective **contraception**, good cycle control and minimal side effects while greatly reducing the total **contraceptive** steroid administered (particularly the oestrogenic component) per **28-day** cycle.

Dwg.0/0

L28 ANSWER 56 OF 61 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-008439 [01] WPIDS
DNC C1998-002917
TI Method of **contraception** - good cycle control and minimal side-effects while greatly reducing the total **contraceptive** steroid administered.
DC B01
IN GAST, M J
PA (AMHP) AMERICAN HOME PROD CORP
CYC 65
PI WO 9741872 A1 19971113 (199801)* EN 18p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AU BA BB BG BR CA CN CU CZ EE GE HU IL IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK TR TT UA UZ VN
AU 9727460 A 19971126 (199813)
ADT WO 9741872 A1 WO 1997-US7089 19970428; AU 9727460 A AU 1997-27460 19970428
FDT AU 9727460 A Based on WO 9741872
PRAI US 1996-646900 19960508
AN 1998-008439 [01] WPIDS
AB WO 9741872 A UPAB: 19980107
Method of **contraception** comprises administration for 23-25 consecutive days: (a) a first phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 mu g **levonorgestrel** (LN) and an **oestrogen** at a daily dosage

equivalent in oestrogenic activity to 10-15 mu g ethinyl oestradiol for 9-
13 days beginning on day 1 of the menstrual cycle, where the same dosage is administered in each of the 9-**13 days** ; (b) a second phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 mu g LN and an **oestrogen** at a daily dosage equivalent in oestrogenic activity to 10-20 mu g ethinyl oestradiol for **11-15 days** beginning on the day immediately following the last day of administration of the first phase combination, where the same dosage is administered in each of the **11-15 days**; provided that the daily dosage of the second phase progestin in greater than or equal to the first phase progestin and that the daily dosage of the second phase **oestrogen** is greater than or equal to the daily dosage of the first phase **oestrogen**.

ADVANTAGE - The combination provides good **contraception**, good cycle control and minimal side-effects while greatly reducing the total **contraceptive** steroid administered, particularly the oestrogenic component, per **28-day** cycle.

Dwg.0/0

L28 ANSWER 57 OF 61 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-558683 [51] WPIDS
DNC C1997-178351
TI Method of **contraception** - good cycle control and minimal side-effects while greatly reducing the total **contraceptive** steroid administered.
DC B01
IN GAST, M J
PA (AMHP) AMERICAN HOME PROD CORP
CYC 65
PI WO 9741870 A1 19971113 (199751)* EN 24p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AU BA BB BG BR CA CN CU CZ EE GE HU IL IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK TR TT UA UZ VN
AU 9729268 A 19971126 (199813)
ADT WO 9741870 A1 WO 1997-US7084 19970428; AU 9729268 A AU 1997-29268 19970428
FDT AU 9729268 A Based on WO 9741870
PRAI US 1996-647087 19960508
AN 1997-558683 [51] WPIDS
AB WO 9741870 A UPAB: 19971222
Method of **contraception** comprises administration for **28** consecutive **days**: (a) a first phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 mu g **levonorgestrel** (LN) and an **oestrogen** at a daily dosage equivalent in oestrogenic activity to 10-20 mu g ethinyl oestradiol for 3-8 days beginning on day 1 of the menstrual cycle, where the same dosage is administered in each of the 3-8 days; (b) a second phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 mu g LN and an **oestrogen** at a daily dosage equivalent in oestrogenic activity to 10-20 mu g ethinyl oestradiol for 4-**15 days** beginning on the last day of administration of the first phase combination, where the same dosage is administered in each of the 4-

15 days; (c) a third phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 mu g **levonorgestrel** and an **oestrogen** at a daily dosage equivalent in **oestrogen** ic activity to 10-20 mu g ethinyl oestradiol for 4-**15 days** beginning on the day immediately following the last day of administration of the second phase combination where the same dosage of the progestin and **oestrogen** combination is administered on each of the 4-**15 days**; provided that the daily dosages of the combinations administered in phases one and two are different and in phases two and three are different. Also claimed is a three-phase **contraceptive** kit adapted for daily oral administration comprising 3-8 units comprising (a), 4-15 units comprising (b) and 4-15 unit comprising (c) provided that the daily dosages of the combinations administered in phases one and two are different and in phases two and three are different, so that the total number of dosage units is 23-25, or optionally the kit further comprises 3-5 dosage units each containing a non-**contraceptive** placebo so that the total number of units is 28.

ADVANTAGE - The combination provides good **contraception**, good cycle control and minimal side-effects while greatly reducing the total **contraceptive** steroid administered, particularly the oestrogenic component, per **28-day** cycle.

Dwg.0/0

L28 ANSWER 58 OF 61 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-558682 [51] WPIDS
DNC C1997-178350
TI Method of **contraception** - good cycle control and minimal side-effects while greatly reducing the total **contraceptive** steroid administered.
DC B01
IN GAST, M J
PA (AMHP) AMERICAN HOME PROD CORP
CYC 65
PI WO 9741869 A1 19971113 (199751)* EN 19p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AU BA BB BG BR CA CN CU CZ EE GE HU IL IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK TR TT UA UZ VN
AU 9729267 A 19971126 (199813)
ADT WO 9741869 A1 WO 1997-US7083 19970428; AU 9729267 A AU 1997-29267 19970428
FDT AU 9729267 A Based on WO 9741869
PRAI US 1996-643429 19960508
AN 1997-558682 [51] WPIDS
AB WO 9741869 A UPAB: 19971222
Method of **contraception** comprises administration for **28** consecutive **days**: (a) a first phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 mu g **levonorgestrel** (LN) and an **oestrogen** at a daily dosage equivalent in oestrogenic activity to 10-15 mu g ethinyl oestradiol for 9-**13 days** beginning on day 1 of the menstrual cycle, where the same dosage is administered in each of the 9-**13 days**; (b) a second phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 mu g LN and an

oestrogen at a daily dosage equivalent in oestrogenic activity to 10-20 mu g ethinyl oestradiol for **11-15 days** beginning on the last day of administration of the first phase combination, where the same dosage is administered in each of the **11-15 days**; (c) an **oestrogen** phase **oestrogen** at a daily dosage equivalent in oestrogenic activity to 10-20 mu g ethinyl oestradiol for 3-5 days beginning on the day immediately following the last day of administration of the third phase (sic) combination where the same dosage of the **oestrogen** is administered in each of the 3-5 days; and provided that the daily dosage of the second phase progestin is greater than or equal to the first phase progestin and that the daily dosage of the second phase **oestrogen** is greater than or equal to the daily dosage of the first phase **oestrogen**. Also claimed is a **contraceptive** kit adapted for daily oral administration comprising (a)-(c) as above an provided that the dosage of progestin in each second phase dosage unit is greater than the dosage of progestin in the first phase dosage unit and that the dosage of **oestrogen** in each second phase dosage unit is at least the same as that in each first phase dosage unit, and the total number of dosage units in the kit is 28.

ADVANTAGE - The combination provides good **contraception**, good cycle control and minimal side-effects while greatly reducing the total **contraceptive** steroid administered, particularly the oestrogenic component, per **28-day** cycle.

Dwg.0/0

L28 ANSWER 59 OF 61 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1995-123225 [16] WPIDS
DNC C1995-056194
TI New prepn. for hormone replacement therapy and oral **contraception** - comprising at least one progestogen and at least one **oestrogen**, in which the **oestrogen** dose varies, substantially avoiding blood loss.
DC B01
IN KONINCKX, P R M; KONINCKX, P R M W; KONINCKX, P R M W G
PA (SATU-N) SATURNUS AG
CYC 57
PI WO 9507081 A1 19950316 (199516)* EN 13p
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KE KG KP KR KZ LK LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN
NL 9301562 A 19950403 (199518)
AU 9476952 A 19950327 (199528)
EP 717626 A1 19960626 (199630) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
FI 9601098 A 19960403 (199636)
HU 74452 T 19961230 (199714)
JP 09502194 W 19970304 (199719) 12p
CN 1133011 A 19961009 (199802)
US 5827843 A 19981027 (199850)
AU 9918488 A 19990429 (199928)
AU 708881 B 19990812 (199944)
ADT WO 9507081 A1 WO 1994-EP2997 19940908; NL 9301562 A NL 1993-1562 19930909;

AU 9476952 A AU 1994-76952 19940908; EP 717626 A1 EP 1994-927583 19940908,
WO 1994-EP2997 19940908; FI 9601098 A WO 1994-EP2997 19940908, FI 1996-1098 19960308; HU 74452 T WO 1994-EP2997 19940908, HU 1996-592 19940908; JP 09502194 W WO 1994-EP2997 19940908, JP 1995-508461 19940908; CN 1133011 A CN 1994-193713 19940908; US 5827843 A WO 1994-EP2997 19940908, US 1996-605118 19960604; AU 9918488 A Div ex AU 1994-76952 19940908, AU 1999-18488 19990226; AU 708881 B AU 1994-76952 19940908
FDT AU 9476952 A Based on WO 9507081; EP 717626 A1 Based on WO 9507081; HU 74452 T Based on WO 9507081; JP 09502194 W Based on WO 9507081; US 5827843
A Based on WO 9507081; AU 708881 B Previous Publ. AU 9476952, Based on WO 9507081
PRAI NL 1993-1562 19930909
AN 1995-123225 [16] WPIDS
AB WO 9507081 A UPAB: 19950502
A new prepn. for oral **contraception** comprises at least one progestogen and at least one **oestrogen**. The **oestrogen** dose varies with a periodicity such that blood loss is substantially avoided.

The progestogen comprises **progesterone** (300-900 mg/day), **norethisterone** acetate (0.2-5 mg/day), medroxyprogesterone acetate (1-5 mg/**day**), d-norgestrel (**30**-150 mg/**day**), **desogestrel** (**30**-150 mug/**day**), **norgestimate** (**30**-150 mug/**day**), **cyproterone acetate** (0.2-2 mg/**day**), **gestodene** (**10**-150 mug/**day**), **3-ketodesogestrel** (**10**-150 mug/**day**), drospirenon (0.2-3.0 mg/day) or their combinations thereof.

The **oestrogen** comprises aethinyloestradiol (5-**15** gamma (sic)/**day**), oestradiol valerianate (1-4 mg/day), oestradiol (1-2 mg/day), conjugated **oestrogen** (0.3-1.25 mg/day), oestriol (1-4 mg/day) or their combinations.

USE - The compsns. are also useful for hormone replacement therapy. They may be administered in oral, transdermal, parenteral and/or implantable application forms.

ADVANTAGE - The compsns. include amenorrhoea with negligible blood loss.

Dwg.0/0

L28 ANSWER 60 OF 61 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-012019 [01] WPIDS
CR 1999-189592 [16]
DNN N2000-009262 DNC C2000-002149
TI Transdermal patches for promoting ovulation and providing hormone-replacement therapy in women.
DC A14 A17 A23 A26 A96 B01 B07 D22 P34
IN AUDETT, J; JONA, J; SINGH, N
PA (CYGN-N) CYGNUS INC
CYC 1
PI US 5972377 A 19991026 (200001)* 6p
ADT US 5972377 A CIP of US 1995-473531 19950607, CIP of US 1995-517263 19950821, Cont of US 1996-660024 19960606, US 1998-165526 19981002
FDT US 5972377 A Cont of US 5876746
PRAI US 1996-660024 19960606; US 1995-473531 19950607; US 1995-517263 19950821; US 1998-165526 19981002
AN 2000-012019 [01] WPIDS

CR 1999-189592 [16]
AB US 5972377 A UPAB: 20000105
NOVELTY - Novel transdermal patches for promoting ovulation in women comprise:
(a) backing layer; and
(b) non-acrylate matrix layer underlying (a).
DETAILED DESCRIPTION - Matrix layer comprises mixture of:
(i) 17-deacetyl **norgestimate;**
(ii) skin-permeation enhancer chosen from lactate ester of 1 2-18C aliphatic alcohol and polyethylene glycol monolaurate (PGML); and
(iii) pressure-sensitive adhesive comprising silicone and/or polyisobutylene, adapted to be in diffusional communication with the skin and to administer an ovulation-inhibiting amount of 17-deacetyl **norgestimate.**
ACTIVITY - Ovulation inhibitor; **contraceptive;** hormone replacement.
MECHANISM OF ACTION - Estrogenic; luteinizing hormone release inhibitor; follicle stimulating hormone secretion inhibitor.
USE - Used to promote ovulation and provide hormone-replacement therapy in women (claimed).
ADVANTAGE - Provide sustained release of active agents. 17-deacetyl **norgestimate** inhibits little or no androgenic activity.
Dwg.0/0

L28 ANSWER 61 OF 61 JICST-EPlus COPYRIGHT 2000 JST
AN 920156549 JICST-EPlus
TI **Levonorgestrel**/Ethinyl Estradiol Study of Developmental Toxicity in Rabbits.
AU KWARTA R F JR; HEMM R D; POLLOCK J J
CHRISTIAN M S
USUI T; SUZUKI M
YAGO N
CS Wyeth-Ayerst Research, New York
Argus Research Lab. Inc., Pennsylvania
Teikoku Hormone MFG Co., Ltd., Kawasaki City, JPN
Wyeth (Japan) Corp., Saitama Pref., JPN
SO Oyo Yakuri (Pharmacometrics), (1991) vol. 42, no. 4, pp. 341-349. Journal Code: S0617A (Fig. 2, Tbl. 7, Ref. 14)
CODEN: OYYAA2; ISSN: 0300-8533
CY Japan
DT Journal; Article
LA English
STA New
AB **Levonorgestrel**/ethinyl estradiol (LNG/EE), a combination progestin/**estrogen** oral **contraceptive** was administered orally by gavage to mated New Zealand White (SPF) rabbits during organogenesis to evaluate the potential for producing developmental toxicity (embryo/fetal toxicity and teratogenicity). Dosage levels were 1.6,8.0 and **40**.0mcg/kg/**day**. 1. In does, drug-related effects included significant decreases in body weight gains and food consumption during the first half of the treatment period, gestation **day**(GD) 6-**11**, in the 8.0 and 40.0mcg/kg groups. The decrease in food consumption in the 40.0mcg/kg group persisted during the second half of the treatment period, GD 12-18, and was accompanied by a decrease in defecation. Water consumption was also significantly reduced on GD 6-11 in the 40.0mcg/kg group. 2. In fetuses, body weight, plancental

weight, sex distribution and gross external, visceral and skeletal morphological development were unaffected by drug treatment. (author abst.)

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=> d his

     (FILE 'HOME' ENTERED AT 07:13:00 ON 02 MAR 2000)

     FILE 'HCAPLUS' ENTERED AT 07:13:03 ON 02 MAR 2000
L1             6 S ENDRIKAT J?/AU
L2             4 S DUSTERBERG B/AU
L3             8 S REILHAC P?/AU
L4             0 S L1 AND L2 AND L3
L5            16 S L1-L4
L6             8 S L5 AND (CONTRACEPT? OR GESTAG? OR ?ESTROGEN?)
                 SELECT RN L6 1-8

     FILE 'REGISTRY' ENTERED AT 07:14:16 ON 02 MAR 2000
L7            24 S E1-24

     FILE 'HCAPLUS' ENTERED AT 07:14:24 ON 02 MAR 2000
L8             6 S L6 AND L7
L9             2 S L6 NOT L8
```

Inventor Search

Searched by John Dantzman 308-4488

=> d all

L9 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2000 ACS
AN 2000:127230 HCAPLUS
TI Comparison of efficacy, cycle control, and tolerability of two low-dose oral **contraceptives** in a multicenter clinical study
AU **Endrikat, J.**; **Dusterberg, B.**; Ruebig, A.; Gerlinger, C.; Strowitzki, T.
CS Schering AG, Berlin, Germany
SO Contraception (1999), 60(5), 269-274
CODEN: CCPTAY; ISSN: 0010-7824
PB Elsevier Science Inc.
DT Journal
LA English
CC 2 (Mammalian Hormones)
AB This study compares the **contraceptive** reliability, cycle control, and tolerability of two oral **contraceptive** prepns. contg. 20 .mu.g of ethinyl estradiol combined with either 75 .mu.g of gestodene (EE/GSD) or 150 .mu.g of desogestrel (EE/DSG). Women received the trial prepns. daily for 21 days, followed by a 7-day pill-free interval. **Contraceptive** efficacy, cycle control, and tolerability were evaluated over a period of 12 cycles. Efficacy data of 14,700 treatment cycles (EE/GSD: 7299; EE/DSG: 7401) were obtained from 1476 women (EE/GSD, n = 740; EE/DSG, n = 736). Both prepns. provided effective **contraception** and good cycle control with a similarly low incidence of both spotting and breakthrough bleeding. The spotting rates in both treatment groups decreased from 35.1% (EE/GSD) and 37.5% (EE/DSG) in the first treatment cycle to approx. 10% in the fourth treatment cycle. The spotting incidence as percent of the total no. of cycles was 12.7% for EE/GSD and 14.3% for EE/DSG. The breakthrough bleeding incidence was 5.2% of all cycles for EE/GSD and 6.0% of all cycles for EE/DSG. For 84.7% of the cycles in the gestodene group and for 82.5% of the cycles in the desogestrel group, neither spotting nor breakthrough bleeding were recorded. Overall, the spotting and breakthrough bleeding incidence tended to be lower with EE/GSD than with EE/DSG. However, the difference was not statistically significant. Amenorrhea was recorded in 2.7% of the cycles with EE/GSD and in 2.9% with EE/DSG. Both prepns. were well tolerated and showed a similar pattern of adverse events. More than 83% of the women in both groups either did not gain wt. or lost more than 2 kg. Both prepns. had a beneficial effect on dysmenorrhea. Both regimens provided reliable **contraception** and good cycle control. The incidence of adverse events was relatively low and both prepns. were well tolerated.

=> d all 2

L9 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2000 ACS
AN 1987:169164 HCAPLUS
DN 106:169164
TI The role of pharmacokinetics in preclinical safety studies of synthetic sex steroids
AU Humpel, Michael; **Dusterberg, B.**; Beier, S.; Schuppler, J.; Gunzel, P.; Elger, W.
CS Schering A.-G., Berlin, Fed. Rep. Ger.
SO Contracept. Steroids (1986), 47-65. Editor(s): Gregoire, A. T.; Blye, Richard P. Publisher: Plenum, New York, N. Y.
CODEN: 55SJAD
DT Conference; General Review
LA English
CC 2-0 (Mammalian Hormones)
AB A review and discussion, with 17 refs., of the interrelationship between kinetics and toxicity and its use in the preclin. safety testing of new sex steroids intended for use as **contraceptives.**
ST review sex steroid pharmacokinetics toxicity; **contraceptive** steroid pharmacokinetics toxicity review
IT Toxicology
(of synthetic sex steroids, in human and lab. animal, pharmacokinetics in relation to)
IT Steroids, biological studies
RL: BIOL (Biological study)
(sex, **contraceptives**, pharmacokinetics and toxicity of, in human)
IT **Contraceptives**
(oral, steroidal, pharmacokinetics and toxicity of, in human and lab. animal)

=> d bib abs hitstr 18

L8 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:604135 HCAPLUS
DN 127:272926
TI A 12-month comparative investigation of reliability, cycle control and tolerance with low-dose oral **contraceptives** containing 20 .mu.g ethinylestradiol and either 75 .mu.g gestodene or 150 .mu.g desogestrel
AU Short, M.; **Endrikat, J.**
CS Women's Medical Clinic, Dublin, Ire.
SO New Option Low-Dose Oral Contracept., Proc. Symp. (1996), Meeting Date 1995, 37-47. Editor(s): Lopes, P.; Killick, S. R. Publisher: Parthenon Publishing, Carnforth.
CODEN: 65BPAP
DT Conference
LA English
AB The clin. profile of an oral **contraceptive** is influenced not only by the **estrogen** dose, but also by the progestogen present in the prepn. Progestogens are not all equal, esp. with respect to cycle control, and therefore it can be of value to compare prepns. with the same **estrogen** dose but different progestogens. In this study, **contraceptive** reliability, cycle control and tolerance of an oral **contraceptive** contg. 20 .mu.g ethinylestradiol and 75 .mu.g gestodene were compared with a ref. prepn. contg. the same dose of **estrogen** combined with 150 .mu.g desogestrel. Interim data from 218 women/2495 cycles in the gestodene group and 219 women/2496 cycles in the desogestrel group have been analyzed from a multicenter study which is in progress in six European countries. **Contraceptive** reliability was found to be good with both prepns. One pregnancy occurred in the gestodene group due to intake error and addnl. there was one non-study-related pregnancy which occurred after a volunteer stopped taking the pill. In the desogestrel group there were two pregnancies, one due to intake error and the other due to method failure. With respect to cycle control, there appeared to be a trend towards a lower incidence of intermenstrual bleeding the gestodene group, although this difference did not achieve statistical significance. The cumulative incidence of spotting during the important first three cycles was 3.5% lower in the gestodene group, and, over the first six cycles, it was 7.6% lower than in the desogestrel group. It was noted that the incidence of dysmenorrhea developing during treatment was less (5.5%) in the gestodene group than in the desogestrel group (15.1%). This statistically significant finding needs further evaluation. Body wt. remained relatively const. in both groups, as did blood pressure, with no hypertension being reported for any woman during the course of the study. The incidence of nuisance adverse events was similar in the two groups, with headache, breast tension and nausea the most frequently reported symptoms. In each treatment group, 19 women discontinued because of adverse events. It is concluded that both

prepns. are reliable and well-tolerated oral **contraceptives**.
There is, however, evidence of a trend towards better cycle control in the
gestodene group.

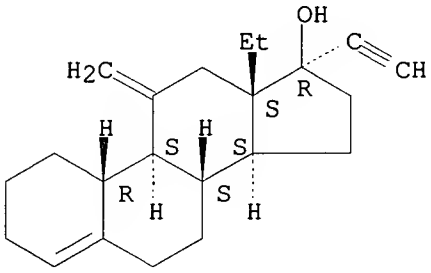
IT **71138-35-7 109852-02-0**, Ethynylestradiol-gestodene mixt.
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(reliability, cycle control and tolerance with low-dose oral **contraceptives** contg. ethinylestradiol and gestodene or desogestrel in women)

RN 71138-35-7 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17.alpha.)-, mixt. with (17.alpha.)-13-ethyl-11-methylene-18,19-dinorpregn-4-en-20-yn-17-ol (9CI) (CA INDEX NAME)

CM 1

CRN 54024-22-5
CMF C22 H30 O

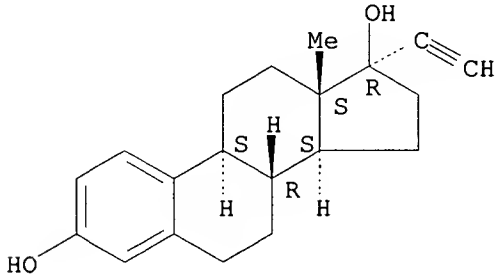
Absolute stereochemistry. Rotation (+).



CM 2

CRN 57-63-6
CMF C20 H24 O2
CDES 4:17A.PREGN

Absolute stereochemistry.

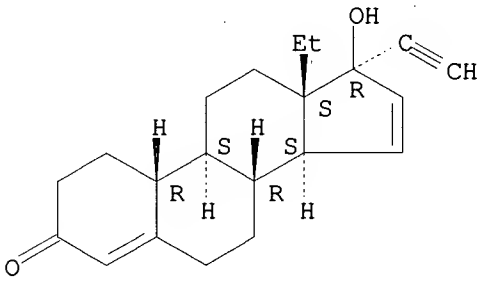


RN 109852-02-0 HCAPLUS
CN 18,19-Dinorpregna-4,15-dien-20-yn-3-one, 13-ethyl-17-hydroxy-, (17.alpha.)-, mixt. with (17.alpha.)-19-norpregna-1,3,5(10)-trien-20-yne-3,17-diol (9CI) (CA INDEX NAME)

CM 1

CRN 60282-87-3
CMF C21 H26 O2
CDES 4:17A.PREGN

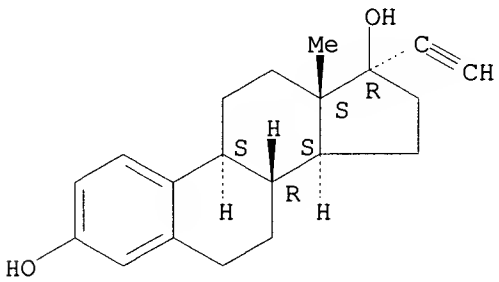
Absolute stereochemistry.



CM 2

CRN 57-63-6
CMF C20 H24 O2
CDES 4:17A.PREGN

Absolute stereochemistry.



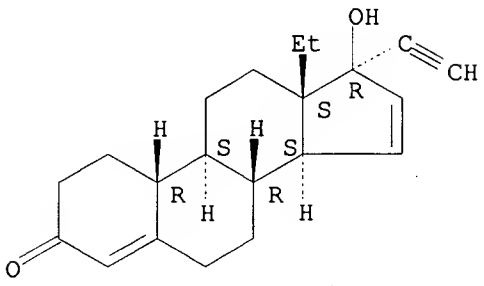
=> d bib abs hitstr l8 2

L8 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:604113 HCAPLUS
DN 127:272925
TI Three years' clinical experience with a new low-dose oral **contraceptive** containing 20 .mu.g ethinylestradiol and 75 .mu.g gestodene: efficacy, cycle control and tolerability
AU **Dusterberg, B.**; Ellman, H.; Muller, U.; Rowe, E.; Muhe, B.
CS Schering AG, Berlin, Germany
SO New Option Low-Dose Oral Contracept., Proc. Symp. (1996), Meeting Date 1995, 21-35. Editor(s): Lopes, P.; Killick, S. R. Publisher: Parthenon Publishing, Carnforth.
CODEN: 65BPAP
DT Conference
LA English
AB While there are theor. advantages assocd. with the continuing redn. of the ethinylestradiol dose in oral **contraceptives**, it is important to be sure that **contraceptive** reliability is not compromised and that good cycle control is maintained. A no. of studies have demonstrated that oral **contraceptives** contg. gestodene are assocd. with particularly good cycle control and therefore it was anticipated that a prepn. contg. 20 .mu.g ethinylestradiol and 75 .mu.g gestodene would prove to be both effective and well tolerated. To investigate this, a long-term, open-label, multicenter study of clin. efficacy and tolerability was undertaken. A total of 670 women between the ages of 18 and 45 yr received the trial prepn. over a 3-yr period, which resulted in 19095 cycles available for evaluation. Only one pregnancy occurred during the study, which was the result of pill intake errors, giving an uncorrected Pearl index of 0.07. Cycle control with the trial prepn. was good, esp. in women who did not miss any pills. By cycle 3, only 10.2% of women who had not missed pills reported inter-menstrual bleeding and this decreased to 2.3% by cycle 36. The prepn. was tolerated, with a low incidence of nuisance adverse events. There were no clin. significant changes in mean body wt. or blood pressure. Over the 3 yr of the study, 10% of women withdrew for reasons related mostly to mild adverse events. From this study demonstrate that this low-dose prepn. contg. gestodene combined with 20 .mu.g ethinylestradiol is a reliable and well-tolerated oral **contraceptive** that provides good cycle control.
IT **109852-02-0**, Ethinylestradiol-gestodene mixt.
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(efficacy, cycle control and tolerability of low-dose oral **contraceptive** contg. ethinylestradiol and gestodene in women)
RN 109852-02-0 HCAPLUS
CN 18,19-Dinorpregna-4,15-dien-20-yn-3-one, 13-ethyl-17-hydroxy-, (17.alpha.)-, mixt. with (17.alpha.)-19-norpregna-1,3,5(10)-trien-20-yne-3,17-diol (9CI) (CA INDEX NAME)

CM 1

CRN 60282-87-3
CMF C21 H26 O2
CDES 4:17A.PREGN

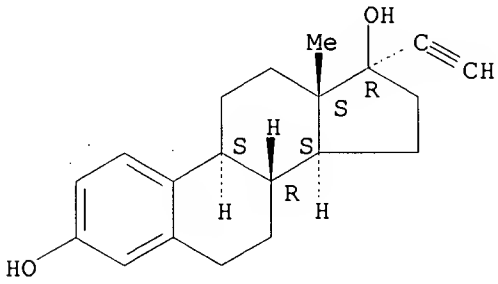
Absolute stereochemistry.



CM 2

CRN 57-63-6
CMF C20 H24 O2
CDES 4:17A.PREGN

Absolute stereochemistry.



=> d bib abs hitstr l8 3

L8 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:465078 HCAPLUS
DN 127:86120
TI Method and kit for **contraception**
IN **Endrikat, Jan**; Duesterberg, Bernd; **Reilhac, Pia**
PA Schering A.-G., Germany
SO Ger. Offen., 7 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19549264	A1	19970626	DE 1995-19549264	19951223
	CA 2241192	AA	19970703	CA 1996-2241192	19961220
	WO 9723228	A2	19970703	WO 1996-DE2486	19961220
	WO 9723228	A3	19970828		
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9719219	A1	19970717	AU 1997-19219	19961220
	EP 868188	A2	19981007	EP 1996-946221	19961220
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1205639	A	19990120	CN 1996-199301	19961220
	BR 9612207	A	19990713	BR 1996-12207	19961220
	JP 2000502108	T2	20000222	JP 1997-523223	19961220
	NO 9802902	A	19980622	NO 1998-2902	19980622
PRAI	DE 1995-19549264		19951223		
	WO 1996-DE2486		19961220		

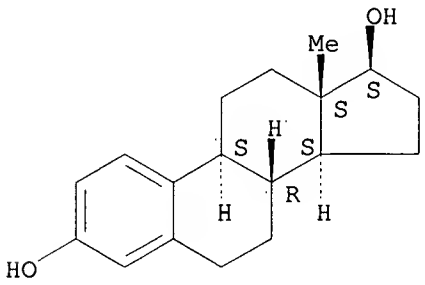
AB A method for **contraception** in female mammals involves administration of an ovulation-inhibiting dose of a **gestagen** daily for .gtoreq.28 days, and of a natural **estrogen** for 5-10 days at the end of this 28-day period. This regimen allows regular menstruation-like bleeding combined with reliable control of the ovarian cycle. The **gestagen** may be administered orally and the **estrogen** transdermally, or vice versa. Alternatively, a kit may comprise a 1st phase of 18-23 daily oral doses of **gestagen** and a 2nd phase of 5-10 daily oral doses of a **gestagen-estrogen** combination. For example, levonorgestrel was administered for 56 days at 0.1 mg/day; during the last 10 days of this period, estradiol was addnl. administered at 2.5 mg/day.

IT **50-28-2**, Estradiol, biological studies **51-98-9**, Norethisterone acetate **57-83-0**, Progesterone, biological studies **68-22-4**, Norethisterone **302-22-7**, Chlormadinone acetate **427-51-0**, Cyproterone acetate **797-63-7**, Levonorgestrel **35189-28-7**, Norgestimate **54024-22-5**, Desogestrel **54048-10-1**, 3-Ketodesogestrel **60282-87-3**, Gestodene **65928-58-7**, Dienogest **67392-87-4**, Drospirenone

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method and kit for **contraception**)

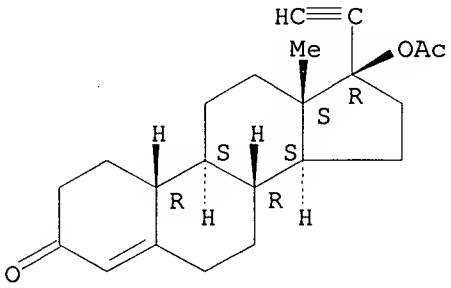
RN 50-28-2 HCAPLUS
CN Estra-1,3,5(10)-triene-3,17-diol (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



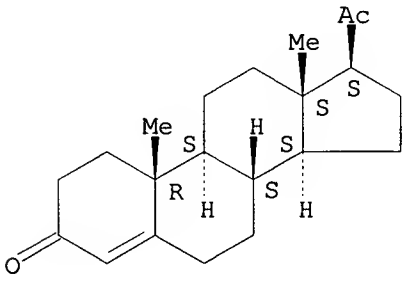
RN 51-98-9 HCAPLUS
CN 19-Norpregn-4-en-20-yn-3-one, 17-(acetyloxy)-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 57-83-0 HCAPLUS
CN Pregn-4-ene-3,20-dione (9CI) (CA INDEX NAME)

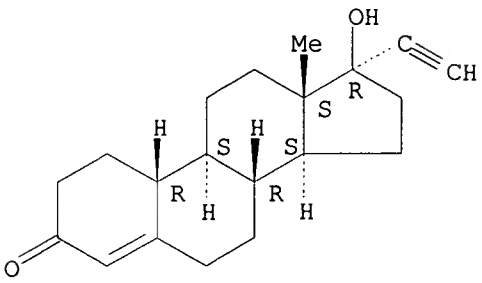
Absolute stereochemistry.



RN 68-22-4 HCAPLUS
CN 19-Norpregn-4-en-20-yn-3-one, 17-hydroxy-, (17.alpha.)- (9CI) (CA INDEX

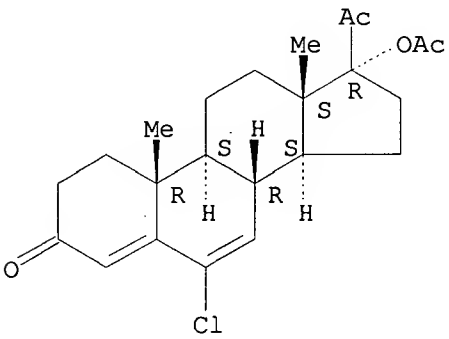
NAME)

Absolute stereochemistry.



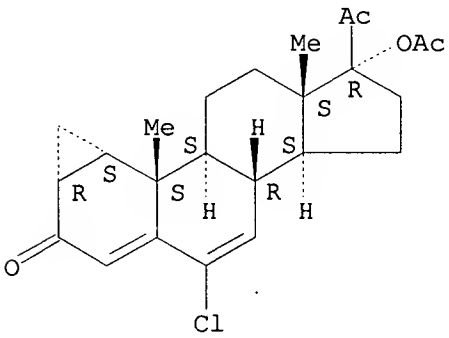
RN 302-22-7 HCAPLUS
CN Pregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



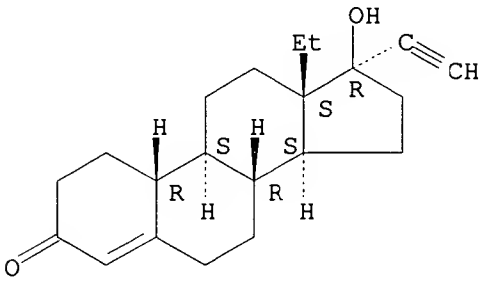
RN 427-51-0 HCAPLUS
CN 3'H-Cyclopropa[1,2]pregna-1,4,6-triene-3,20-dione, 17-(acetyloxy)-6-chloro-
1,2-dihydro-, (1.beta.,2.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



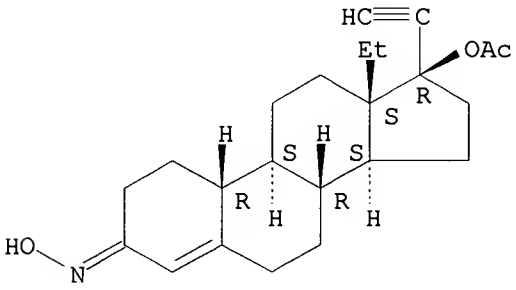
RN 797-63-7 HCAPLUS
CN 18,19-Dinorpregn-4-en-20-yn-3-one, 13-ethyl-17-hydroxy-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



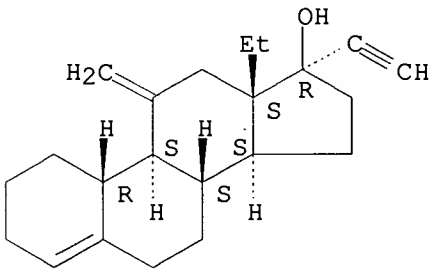
RN 35189-28-7 HCAPLUS
CN 18,19-Dinorpregn-4-en-20-yn-3-one, 17-(acetyloxy)-13-ethyl-, 3-oxime, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 54024-22-5 HCAPLUS
CN 18,19-Dinorpregn-4-en-20-yn-17-ol, 13-ethyl-11-methylene-, (17.alpha.)- (9CI) (CA INDEX NAME)

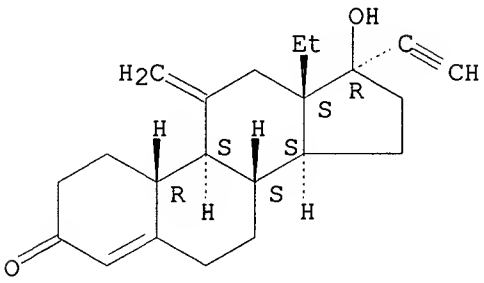
Absolute stereochemistry. Rotation (+).



RN 54048-10-1 HCAPLUS
CN 18,19-Dinorpregn-4-en-20-yn-3-one, 13-ethyl-17-hydroxy-11-methylene-,

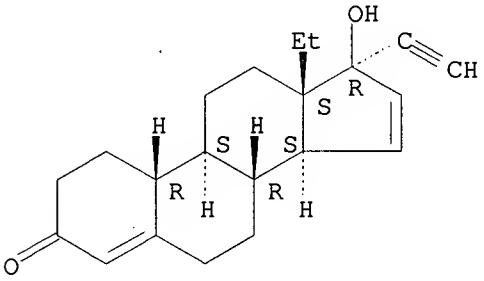
(17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



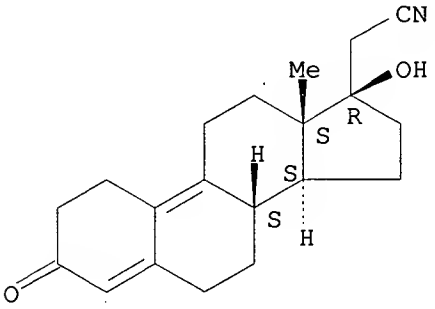
RN 60282-87-3 HCAPLUS
CN 18,19-Dinorpregna-4,15-dien-20-yn-3-one, 13-ethyl-17-hydroxy-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 65928-58-7 HCAPLUS
CN 19-Norpregna-4,9-diene-21-nitrile, 17-hydroxy-3-oxo-, (17.alpha.)- (9CI) (CA INDEX NAME)

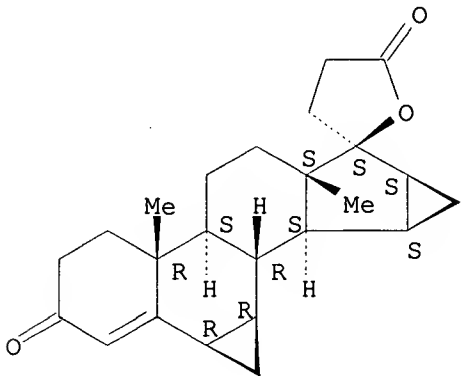
Absolute stereochemistry.



RN 67392-87-4 HCAPLUS
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-, (2'S,6R,7R,8R,9S,10R,13S,14S,15S,16S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d bib abs hitstr l8 4

L8 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:307252 HCAPLUS
DN 126:338964
TI A twelve-month comparative clinical investigation of two low-dose oral **contraceptives** containing 20 .mu.g ethinylestradiol/75 .mu.g gestodene and 30 .mu.g ethinylestradiol/75 .mu.g gestodene, with respect to efficacy, cycle control, and tolerance
AU **Endrikat, J.**; Mueller, U.; Duesterberg, B.
CS Schering AG, Berlin, D-13342, Germany
SO Contraception (1997), 55(3), 131-137
CODEN: CCPTAY; ISSN: 0010-7824
PB Elsevier
DT Journal
LA English
AB The aim of this study was to compare **contraceptive** reliability, cycle control, and tolerance of an oral **contraceptive** contg. 20 .mu.g ethinylestradiol (EE2) and 75 .mu.g gestodene (GSD), with a ref. prepn. contg. a similar dose of gestodene but in combination with 30 .mu.g ethinylestradiol. A higher incidence of intermenstrual bleeding was apparent under the 20 .mu.g EE2 oral **contraceptive**. For the 20 .mu.g EE2 prepn., 47.4% of all women reported spotting at least once over a period of 12 treatment cycles, whereas this figure was 35.5% for the 30 .mu.g EE2 pill. However, the incidence was within a range that corresponds to that of other OCs. The cumulative breakthrough bleeding rates (at least once during the one year of treatment) of 14.5% (20 .mu.g EE2) and 11.8% (30 .mu.g EE2) of women were not significantly different. In relation to all cycles, the intermenstrual bleeding rates were remarkably lower, indicating that the majority of the volunteers experienced such events only in few cycles under treatment: the spotting rate was 11.5% (20 .mu.g EE2) and 7.2% (30 .mu.g EE2) of all cycles, and the break-through bleeding rate was 2.6% and 1.6% of all cycles, resp. Three pregnancies were recorded during the study (one in the 20 .mu.g EE2+75 .mu.g GSD group, two in the 30 .mu.g EE2+75 .mu.g GSD group). All three could be explained either by intake irregularities or by circumstances impairing the **contraceptive** effect. The influence of both treatments on the blood pressure and body wt. proved to be extremely slight. Adverse events in both groups were rare and differences in the frequency of adverse events were not apparent. The discontinuation rate due to adverse events, including intermenstrual bleeding, was low (9.8% for 20 .mu.g EE2+75 .mu.g GSD, and 7.2% for 30 .mu.g EE2+75 .mu.g GSD) and was in the lower range known for other oral **contraceptives**. Both prepns. were well accepted by the volunteers. The data obtained demonstrate clin. acceptable cycle control, good tolerance, and a high std. of **contraceptive** reliability for both drugs. Prescription of the 20 .mu.g EE2 prepn. could be the first-line therapy to provide the lowest amt. of EE2 possible. In case of persistent cycle control problems, a switch to the 30 .mu.g EE2 drug should be considered.

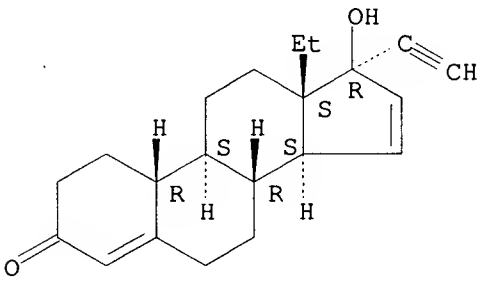
Searched by John Dantzman 308-4488

IT **109852-02-0**, Ethinylestradiol-gestodene mixt.
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(efficacy, cycle control, and tolerance of ethinylestradiol-gestodene oral **contraceptive** in relation to **estrogen** and progestogen dose in women)
RN 109852-02-0 HCAPLUS
CN 18,19-Dinorpregna-4,15-dien-20-yn-3-one, 13-ethyl-17-hydroxy-, (17.alpha.)-, mixt. with (17.alpha.)-19-norpregna-1,3,5(10)-trien-20-yne-3,17-diol (9CI) (CA INDEX NAME)

CM 1

CRN 60282-87-3
CMF C21 H26 O2
CDES 4:17A.PREGN

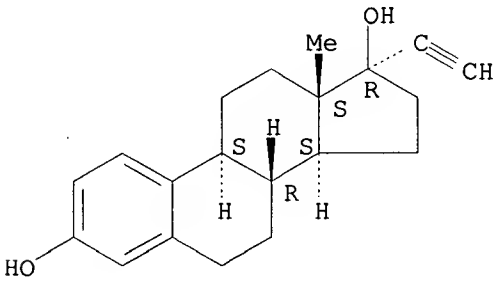
Absolute stereochemistry.



CM 2

CRN 57-63-6
CMF C20 H24 O2
CDES 4:17A.PREGN

Absolute stereochemistry.



=> d bib abs hitstr 18 5

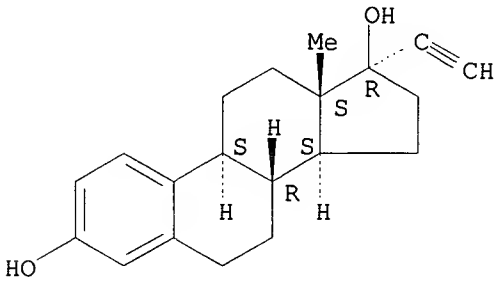
L8 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:176424 HCAPLUS
DN 124:220782
TI A comparative study of the effects of the hemostatic system of two monophasic gestodene oral **contraceptives** containing 20 .mu.g and 30 .mu.g ethinylestradiol
AU Winkler, U. H.; Schindler, A. E.; **Endrikat, J.**; Duesterberg, B.
CS University Hospital Essen, Essen, Germany
SO Contraception (1996), 53(2), 75-84
CODEN: CCPTAY; ISSN: 0010-7824
DT Journal
LA English
AB The effects of two oral **contraceptives**, contg. gestodene and either 20 .mu.g or 30 .mu.g ethinylestradiol, on hemostatic parameters was investigated in a six-month randomized study involving a total of 40 healthy women between the ages of 18 and 30 yr. A large no. of hemostatic parameters were measured, which were categorized as either pro-coagulatory, anti-coagulatory, profibrinolytic, anti-fibrinolytic or indicative of fibrin turnover. Addnl., tissue plasminogen activator (t-PA) and plasminogen activator inhibitor (PAI-1) were measured before and after venous occlusion and delta and ratio values calcd. Pro-coagulatory factors as well as reaction products reflecting in vivo coagulatory activity (thrombin-antithrombin III complex, prothrombin fragment 1+2) were found to increase. Among the anti-coagulatory parameters, only protein S concn. and protein S activity decreased, most notably in the 30 .mu.g EE group. There was a corresponding increase in fibrinolytic activity reflected by reaction products of in vivo fibrinolysis (plasmin-antiplasmin 2-complex, fibrin-degrdn. products). Measurement of t-PA and PAI-1, before and after venous occlusion, revealed that the fibrinolytic response was more pronounced in the 20 .mu.g EE group. There was also an increase in the threshold of fibrinolytic inhibition (ratio PAI-1) in both groups, which was less pronounced in the 20 .mu.g EE group. Apart from isolated measurements, all parameters remained within their normal ranges and values returned to baseline in the follow-up cycle. It is concluded that both prepns. had a balanced effect on the hemostatic system stimulating both pro-coagulant and fibrinolytic activity. No statistically significant differences were obsd. between the two groups; however, there was a trend towards greater fibrinolytic capacity in the 20 .mu.g EE group.
IT **9049-68-7D**, Antiplasmin, complexes with plasmin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(2; monophasic gestodene oral **contraceptives** contg. different ethinylestradiol doses effect on hemostatic system in women)
RN 9049-68-7 HCAPLUS
CN Plasmin inhibitor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **57-63-6**, Ethinylestradiol **60282-87-3**, Gestodene

109852-02-0, Gestodene-ethinylestradiol mixt.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monophasic gestodene oral **contraceptives** contg. different ethinylestradiol doses effect on hemostatic system in women)

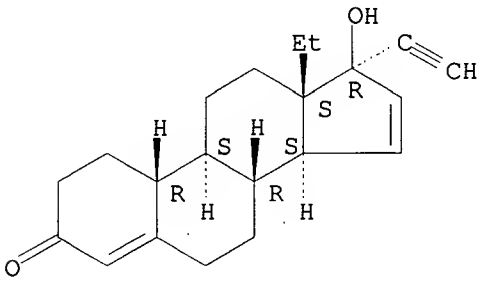
RN 57-63-6 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 60282-87-3 HCAPLUS
CN 18,19-Dinorpregna-4,15-dien-20-yn-3-one, 13-ethyl-17-hydroxy-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

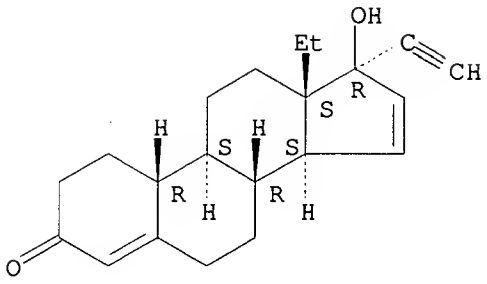


RN 109852-02-0 HCAPLUS
CN 18,19-Dinorpregna-4,15-dien-20-yn-3-one, 13-ethyl-17-hydroxy-, (17.alpha.)-, mixt. with (17.alpha.)-19-norpregna-1,3,5(10)-trien-20-yne-3,17-diol (9CI) (CA INDEX NAME)

CM 1

CRN 60282-87-3
CMF C21 H26 O2
CDES 4:17A.PREGN

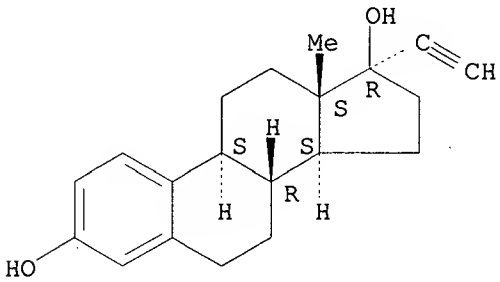
Absolute stereochemistry.



CM 2

CRN 57-63-6
CMF C20 H24 O2
CDES 4:17A.PREGN

Absolute stereochemistry.



IT **9000-94-6D**, Antithrombin III, complexes with thrombin
9001-90-5D, Plasmin, complexes with antiplasmin 2
9002-04-4D, Thrombin-, complexes with antithrombin III
72270-84-9, Prothrombin fragment 1 **78768-79-3**,
Prothrombin fragment 2 **139639-23-9**, Tissue plasminogen activator
140208-23-7, Plasminogen activator inhibitor 1
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(monophasic gestodene oral **contraceptives** contg. different ethinylestradiol doses effect on hemostatic system in women)
RN 9000-94-6 HCAPLUS
CN Antithrombin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-90-5 HCAPLUS
CN Plasmin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9002-04-4 HCAPLUS
CN Thrombin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 72270-84-9 HCAPLUS
CN Blood-coagulation factor II, fragment 1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 78768-79-3 HCAPLUS
CN Blood-coagulation factor II, fragment 2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 139639-23-9 HCAPLUS
CN Plasminogen activator, tissue-type (9CI) (CA INDEX NAME)

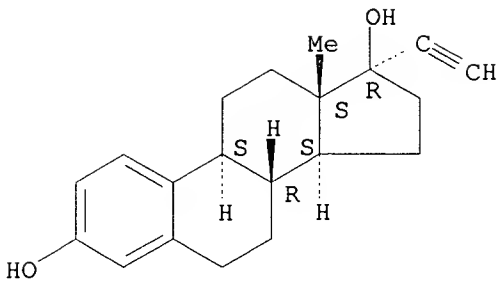
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 140208-23-7 HCAPLUS
CN Proteinase inhibitor, PAI-1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d bib abs hitstr l8 6

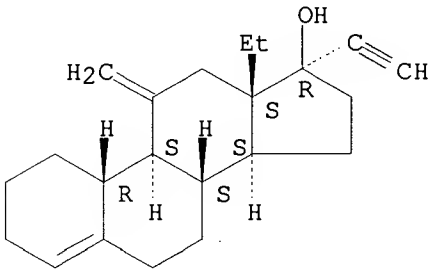
L8 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:940912 HCAPLUS
DN 124:45916
TI A twelve-month comparative clinical investigation of two low-dose oral **contraceptives** containing 20 .mu.g ethinylestradiol/75 .mu.g gestodene and 20 .mu.g ethinylestradiol/150 .mu.g desogestrel, with respect to efficacy, cycle control and tolerance
AU **Endrikat, J.**; Jaques, M. -A.; Mayerhofer, M.; Pelissier, C.; Mueller, U.; Duesterberg, B.
CS Schering AG, Berlin, D-13342, Germany
SO Contraception (1995), 52(4), 229-35
CODEN: CCPTAY; ISSN: 0010-7824
DT Journal
LA English
AB The aim of this study was to compare **contraceptive** reliability, cycle control and tolerance of an oral **contraceptive** contg. 20 .mu.g ethinylestradiol and 75 .mu.g gestodene, with a ref. prepn. contg. the same dose of **estrogen** combined with 150 .mu.g desogestrel. This article presents interim data from centers in France and Austria, involving a total of 479 women and 4,991 cycles. **Contraceptive** reliability was good with both prepns. With respect to cycle control, there is a trend towards a lower incidence of intermenstrual bleeding in the gestodene group. The incidence of spotting (scanty bleeding) during the important first three cycles was 3.5% lower in the gestodene group, and over the first six cycles, it was 7.6% lower. Amenorrhea was similar in both groups, but the incidence of dysmenorrhea was significantly lower in the gestodene group ($p = 0.001$). Adverse events were similar in both groups, with headache, breast tension and nausea the most frequently reported symptoms. Body wt. remained relatively const. during treatment in both groups, and no hypertension was reported for any woman during the course of the study. In each treatment group, 19 women discontinued because of adverse events. It is concluded that both prepns. are reliable and well tolerated oral **contraceptives**; however, there is a more favorable effect on dysmenorrhea by the gestodene formulation.
IT **57-63-6**, Ethinylestradiol **54024-22-5**, Desogestrel **60282-87-3**, Gestodene
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(efficacy, cycle control and tolerance of low-dose oral **contraceptives** contg. 20 .mu.g ethinylestradiol/75 .mu.g gestodene and 20 .mu.g ethinylestradiol/150 .mu.g desogestrel in humans)
RN 57-63-6 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



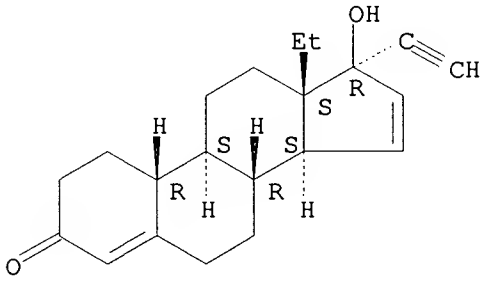
RN 54024-22-5 HCAPLUS
CN 18,19-Dinorpregn-4-en-20-yn-17-ol, 13-ethyl-11-methylene-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 60282-87-3 HCAPLUS
CN 18,19-Dinorpregna-4,15-dien-20-yn-3-one, 13-ethyl-17-hydroxy-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d bib abs hitrn 4

L16 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 1993:161077 HCAPLUS
DN 118:161077
TI Female sex hormones. **Estrogen-gestagen** combinations
AU Neumann, Friedmund
CS Berlin, W-1000/65, Germany
SO Pharm. Ztg. (1992), 137(34), 9-15
CODEN: PHZIAP; ISSN: 0031-7136
DT Journal; General Review
LA German
AB A review, with 8 refs., which described the applications of **estrogen**-progestagen drug combination in gynecol., both for contraception and for the treatment of various disorders such as **premenstrual** syndrome, endometriosis, abortion prophylaxis, etc. Historical events in the development of contraceptives and their mechanisms of action, application forms, and risks and side effects are also described.

=> d bib abs hitrn 7

L16 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 1975:68681 HCAPLUS
DN 82:68681
TI Accurate comparative study on the side effects of different pills in the same group of patients
AU El-Sherbini, Abbas
CS Fac. Med., Cairo Univ., Cairo, Egypt
SO Ain Shams Med. J. (1974), 25(4), 579-85
CODEN: AIMJA9
DT Journal
LA English
AB Four oral contraceptives, Volidan [8064-66-2], Lyndiol [8015-14-3], Gynanovlar [**8015-12-1**], and Ovulen [8056-92-6], were given to the same group of patients for 4 successive cycles each and side effects were compared. A significant increase in spotting was obsd. during the 1st 2 cycles with all 4 prepns., but Volidan produced the highest frequency. Break through bleeding was more frequent with Ovulen and Volidan than with the other 2. All 4 prepns. significantly decreased menstrual loss and **premenstrual** tension and dysmenorrhea. Ovulen caused the highest incidence of vomiting and nausea. Gynanovlar and Lyndiol and, to a lesser extent, Ovulen increased body wt. The importance of improving **estrogen-gestagen** balance in the pill rather than diminishing either was discussed.
IT **8015-12-1**
RL: PRP (Properties)
(side effects of)